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MODERN MANAGEMENT OF CANCER OF THE LOWER GASTROINTESTINAL TRACT

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THE past three decades have seen exceptional progress in surgical endeavors directed against cancer of the lower portion of the gastrointestinal tract. The steady and unimpeded advance of the past strengthened by the accumulation and correlation of satisfactory data of the present has faltered only occasionally and has gone forward slowly step by step. From the early elementary though ingenious attempts of the pioneers to treat minor lesions of the anal canal down to such formidable operations as segmental or total colectomy, or the heroic radical combined abdominoperineal resection of the rectum in one stage is a far step. Long years of conscientious endeavor buttressed by fortitude and ingenuity have in our generation flowered to establish surgical procedures for definite pathological lesions of the colon and rectum on a basis which views mortality figures and end-results following such efforts with prideful optimism, especially when compared to similar maneuvers executed elsewhere in the gastrointestinal tract. Advances in technique naturally are spectacular in proportion as they approach perfection, but increased knowledge of the pathological and clinical features of lesions when they go hand in hand with therapeutic measures emphasize steady progress.

The earliest operations on the lower gastrointestinal tract naturally were on the anal canal, because lesions in this locality were easily viewed and accessible for surgical attack. Historical data reviewing evolution of local operation and the progress from these procedures to decompression measures and finally to excision of the rectum for cancer are interesting and useful. Although surgery for cancer of the rectum was first proposed by Morgagni at the beginning of the eighteenth century, it was not until 1739 that the initial operation of posterior proctectomy was performed by Faget. Between that time and the first successful posterior resection without colostomy which was performed by Lisfranc, in 1836, 100 years had elapsed, illustrating how slow was progress in treating rectal cancer until abdominal surgery permitted colostomy and radical attack. Many various forms of local excision which remove the coccyx and even a portion of the sacrum and, to which the names of many master surgeons including Velpeau, Kocher, Kraske, and Hochenegg are attached, stud the literature of the late nineteenth century. Actually local excision of rectal cancer was not very successful in attacking this disease, and it was not until the establishment of colostomy as a necessary part of the procedure that even a small number of

satisfactory results began to be reported. Review of the history of colostomy from the time it was first recorded by Aurelianus as having been performed for ileus by Prazagoras, 400 years before Christ, down to the modern type of colostomy would be tedious and time consuming. Suffice it to say that Littre, in 1710, through the medium of a child who died of a congenital obstruction of the rectum conceived the idea of a permanent colostomy, although it was not until 83 years later that Duret performed a left iliac colostomy for a similar lesion. Another French surgeon, Amussat, established the principle of colostomy for rectal cancer.

Ward, in 1865, probably was the first to advocate routine lumbar colostomy in all cases of rectal cancer showing that the gradual recognition of this maneuver as an integral part of the treatment was slow in developing, due largely to the refusal of the medical profession to accept an artificial anus.

As time went on mortality figures remained high and long range cures continued to result in only a small group of cases. Finally with the development of anesthesia, aseptic surgery and a better understanding of the fundamental principles of surgery as applied in this field, it came about that Miles developed the technique, which today unquestionably gives sufferers from rectal cancer a better chance of longevity than any other. Because the trend in the treatment of rectal cancer has been toward the Miles' operation, it is not perhaps amiss to note here that this extremely radical procedure which most master surgeons today recognize as combining the basic fundamentals of surgical attack on cancer of the rectum, is the result of the work of many men.

Czerny, in 1883, performed the first one stage perineoabdominal resection of the rectum. Finding it impossible to remove a carcinoma well up in the rectum by the perineal route as planned, he promptly and courageously opened the abdomen and completed the resection transperitoneally.

From this time until the announcement of Miles' monumental contribution to the surgery of rectal cancer many procedures have been tried and many modifications of Miles' technique have been instituted, and it is a tribute to Miles, Czerny, and others who developed this operation that the trend both in America and on the Continent is definitely in its favor when it is at all applicable with reasonable mortality. The acceptance of colostomy as a step in surgery for rectal cancer is rarely now disputed. It is true that there remain a few surgeons who debate this thesis and who insist on attempting to perform a type of operation which will save the magnificent sphincteric mechanism of nature. To them I would venture the suggestion that a careful scrutiny of the end-results of such procedures is definitely in order and, I hazard the opinion, that comparison of a group of patients operated by this method with a group of patients receiving the advantages of a radical operation which includes colostomy, will establish the superiority of the latter maneuver. I would not be understood as wholly condemning sphincter saving operations, for indubitably if the cancer has not metastasized but is still local and of a low grade, such a procedure may occasionally be indulged in with satisfaction. However, I know of no way of actually determining prior to resection whether or not malignant cells have escaped to other parts and organs of the body.

Although radical operative procedures which remove areas of gland bearing tissues in the neighborhood of the original growth are always highly desirable, it should be noted that one may not apply a single operative procedure routinely. A surgeon who is capable of performing only one technical maneuver for rectal cancer is not sufficiently versatile to combat the many difficulties which this type of surgery develops. Unquestionably the operation of Mummery which consists of colostomy and posterior resection has a definite field of usefulness in the armamentarium of all surgeons. Moreover, I believe an occasional local excision, because of reasons other than local conditions may be justified; even an occasional segmental resection with anastomosis can be defended. All of which indicates that there are at least two operations, Miles' and Mummery's, by which most rectal cancers may be operated upon and that there are several less radical procedures which, if included in

the surgeon's repertoire, will extend the field of operability advantageously.

Surgery of the colon proper, necessarily awaited full development until the Listerian era, which followed the discovery of anesthesia and permitted fearless invasion of the peritoneal cavity.

In the beginning colostomy as a decompressive measure was about the only operation performed for cancer, but gradually hardy and persistent surgeons doggedly extended the horizon and began attempts at removal of malignant lesions with re-establishment of the gastrointestinal continuity.

As far back as 1823, Reybard, successfully resected the sigmoid flexure for cancer and made a primary anastomosis in a young man 29 years of age. Progress was slow thereafter, although Thiersch reported a resection of the colon for acute obstruction in 1843. Thirty-seven years later only 10 resections of the large bowel had been recorded and only 3 of these were successful. During the nineties, however, more resections were performed successfully because of the development of the principle of exteriorization.

The discovery that a mobile segment of bowel harboring a cancer could be brought outside the peritoneal cavity and having the abdominal wall snugly closed around it remain *in situ* for subsequent resection marked an enormous advance in colonic surgery. This epoch making discovery decreased mortality figures hugely and gave great impetus to a field hitherto viewed with scant interest.

Many names are associated with this type of operation, and heretofore I have thought that Bloch, of Copenhagan, deserved credit for the first account of it published in 1891. However, I am now indebted to Dr. John H. Gibbon, Jr., of Philadelphia, for some information which had escaped my attention.

In a paper before the American Surgical Society in May, 1941, he credits Thomas Bryant as being the first surgeon to bring a loop of bowel containing a carcinoma outside the abdominal cavity and suture the wound around it. Zachary Cope refers to Mr. Bryant in his article entitled "Extra-abdominal Resection of the Colon."[1] The article by Mr. Bryant was published in *The Proceedings of the Royal Medical and Chirurgical Society* (London, 1882, 9: 149), and *The British Medical Journal* (1882, 1: 461).

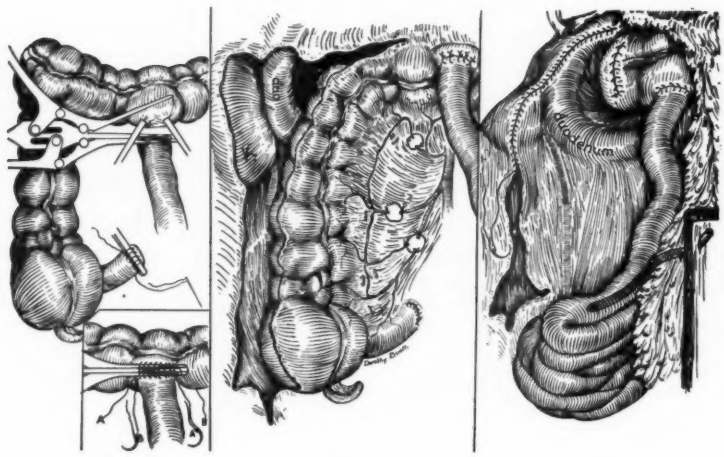
Dr. Gibbon also informs me that an American surgeon, J. M. Barton, of Philadelphia, published an article under the title "Cases of Abdominal Surgery; 13th Case, Resection at Ileocecal Valve for Epithelioma—Recovery" in the *Journal of the American Medical Association* (1888, 10: 549), describing a procedure which embodied the exteriorization principle. Subsequent to these resections, Bloch, in 1891, published a report of his type of resection.

In 1892, Recluse, collaborating with Forgue, published a description of 2 cases of exteriorization of the bowel without mentioning Bloch's name. Paul, of Liverpool, 9 years later, published a modification of Bloch's method, by which he ligated the mesocolon, abutted the two limbs of bowel and decompressed the proximal loop with a glass tube. In 1902, Mikulicz spoke of the procedure which he claimed to have performed first in 1886, and for some reason his name has been commonly attached to all exteriorization operations by surgeons in this country. As a matter of fact, exteriorization represents the concepts of many surgeons, for a single isolated procedure only occasionally marks the discovery of a principle. Even more rarely is the discovery of a principle the work of one man, for research and recorded experiences combine to establish truth and exteriorization may well be said to be an ensemble of principles marking a new era in colonic surgery.

While mortality figures were enormously increased by the discovery of this principle, further progress was insured when the recognition of the principle of decompression prior to resection became universal.

Present day knowledge of the physiology of obstruction easily explains why a sick, dehydrated, and desiccated patient with an imbalanced blood chemistry is such a high risk for any formidable procedure. In consequence, it has come about that a period of preliminary decompression and rehabilitation has become a standardized practice in dealing with large bowel cancer. Such a period has for a long time been part of the attack on ob-

[1]Proc. Royal Soc. Med., 1940, 33: 249.



a b c

Fig. 1. The step in aseptic end-to-side anastomosis between the transverse colon and the terminal ileum. The anastomosis is made first as in a, and then decision is made as to a one stage or two stage procedure. b, Shows mobilization of the right colon. The right kidney and duodenum are demonstrated. c, Shows completion of the operation with peritonealization of raw surfaces. An enterostomy has been done 20 centimeters, from the anastomosis. This step may now be abandoned and the Miller-Abbott tube utilized.

struction from gastroduodenal lesions, obstruction in the urinary tract, and other ailments which cause a profound physiological upset. Applied to lesions of the colon, this principle has been no less emphatically advantageous and, today it is an unwary surgeon who neglects this very necessary phase of the surgical attack.

When one is confronted with a combination of acute intestinal obstruction and cancer, obviously disregard of the malignancy and attack on the acute intestinal obstruction is the proper sequence. How often this principle is modified or reversed in attack on the two ailments combined is an unforgettable error of judgment reflected in mortality statistics. Although cancer of the colon, particularly of the left colon, in the vast majority of cases produces some type of intestinal obstruction, acute, subacute, or chronic, one may, save in the acute variety always attempt medical decompression and with splendid chances of success. When the obstruction must be relieved surgically a cecostomy without exploration is the procedure of choice. This acute intestinal obstruction while usually due to malignancy, more than occasionally is the result of injudicious administration of opaque media by mouth, a procedure to be entirely condemned as not only useless in the diagnosis of colonic lesions, but definitely dangerous in the presence of encircling neoplasms of the left colon.

Recently I have studied a group of cases of cancer of the colon and rectum which occurred in my private practice from February 1, 1933, to February 1, 1940. This group occurred in a series of 605 cases diagnosed as major lesions of the lower gastrointestinal tract. Of these major lesions 418 patients had cancer, thus emphasizing the fact that practically 2 out of 3 of the major organic lesions of the colon and rectum are due to cancer. There were diagnosed 178 cases of cancer of the right and left colon; 100 males and 78 females: 170 were operated upon.

Table I shows the type of operation used for cancer of the colon, the resectability percentages, and the mortality figures. Operative technique and the question of type of operation must vary in the two halves of the colon because of differences in physiology, pathology,

TABLE 1.—ANALYSIS OF 170 CASES

Operations for cancer of the left colon	Cases	Deaths	Per cent Mortality
Obstructive resection and cecostomy (1 or 2 stages)	59	6	
Exteriorization	38	4	
Aseptic anastomosis and resection (cecostomy)	2	1	
Exploration alone or with decompression	37	3	
	136	14	10.2

Cases.....136
Operations...163 Resectability...72 per cent
Resections... 98

Operations for cancer of the right colon			
Ileocolostomy and resection, 1 stage	10	5	
Ileocolostomy and resection, 2 stages	14	0	
Colectomy and ileosigmoidostomy, (2 stages)	1	0	
Ileocolostomy	9	1	
	34	6	17.5

Cases..... 34
Operations.... 49 Resectability...73.5 per cent
Resections.... 25

and anatomy. As a general principle it is safe to assume that cancer of the right colon may be extirpated most satisfactorily by an ileocolostomy and resection in one or two stages.

Aseptic ileocolostomy between the terminal ileum and the middle of the transverse colon followed immediately or at a later stage by resection is the procedure of choice. My apostasy from an open type of anastomosis dates back 15 years or more when I developed an instrument for performing an aseptic anastomosis. In consequence, I am convinced of its utility in avoiding or at least reducing infection and certainly the simplicity of its performance recommends it to most surgeons. Nevertheless, in the modern management of colon cases and with the new chemotherapeutic agents available to sterilize the bowel, one may be quite justified in doing an open anastomosis if that is deemed preferable. An anastomosis between small and large bowel by whatever technique one chooses to do it is a relatively satisfactory procedure in so far as healing is concerned. The blood supply of the small bowel is copious, and that of the large bowel, while less free, is definitely adequate and usually of a constant pattern. Leakage at the anastomosis line is rare, and

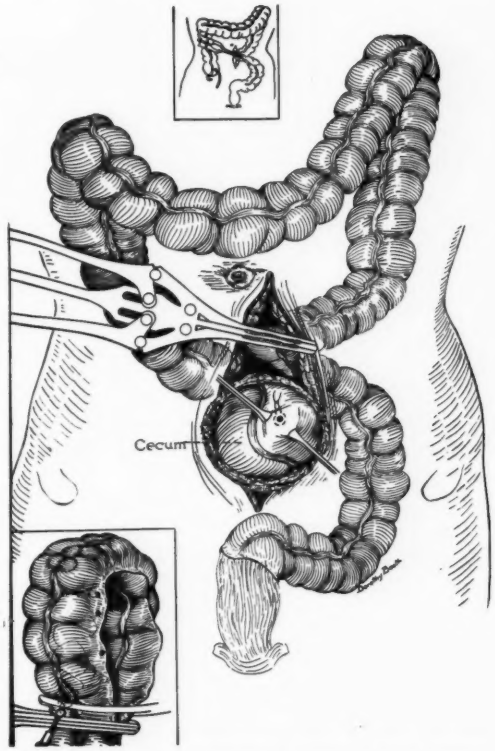


Fig. 2. Steps in obstructive resection plus complementary cecostomy. The addition of the cecostomy which required very little time has been a very valuable adjunct.

when resection is done by modern types of technique is almost a unique occurrence.

Exteriorization procedures in the right colon I definitely deprecate for three reasons: (1) infection around the growth secondary to obstruction and ulceration is likely to produce a lethal peritonitis from the efforts at mobilization; (2) few circumstances are more unpleasant to a convalescent patient than a deluge of liquid alvine discharges over the abdominal wall; (3) it takes little extra time to do some type of anastomosis, and a patient who will tolerate an exteriorization will usually tolerate an anastomosis and thereby avoid the unpleasantness of an artificial stoma.

The mortality in the right colon in this small series indicates that a two stage procedure often is advantageous. In reviewing the 5 deaths which occurred following single

stage operation it is not apparent that a different type of technique would have resulted differently. One individual was an elderly person of 70, in good condition and with a freely movable right colonic cancer. She died 14 days after operation. Another individual was a middle age woman of 50, with 2 cancers, one in the rectosigmoid and one in the right colon. An ileocolostomy sidetracking the right colonic cancer as the first stage of a graded maneuver was performed. She died 3 weeks later of a subphrenic abscess. A third death in this series was due to leakage at the anastomosis.

Nevertheless I believe that there frequently are instances when it is desirable to use ileocolostomy and resection in one stage. More often I think it is desirable to do the operation in two stages. A question of ileostomy for decompression after primary anastomosis and resection seems to be satisfactorily solved at present by the utilization of the Miller-Abbott tube. This tube does all that ileostomy can do and even more and avoids the unpleasantness of ileostomy as well as additional surgery.

In the left colon it will be noted that the choice of operation was obstructive resection and cecostomy. Usually the cecostomy is employed as a complement to the resection. Occasionally, when a patient has an obstruction, it is utilized prior to resection as a decompressive measure. In 59 patients operated upon by this maneuver there were 6 deaths; a mortality of 10.1 per cent.

I have been reticent to accept the principle of primary anastomosis in lesions of the left and transverse colon, because the mortality in my hands has been higher and, I have not been sure that I could do as radical a resection and immediate anastomosis as by resection and delayed union. I have no quarrel with surgeons who choose resection and primary anastomosis and feel sure that it is frequently indicated when the preliminary efforts at decompression have been adequate. On the other hand, I think the crux of the situation lies in the radical removal of mesentery and adjacent gland bearing tissues.

In considering immediate restoration of intestinal continuity economic factors must not be allowed to influence surgical judgment, nor must the desire to perform an artistic surgical operation be considered favorably against a radical, even mutilating type of procedure in dealing with cancer.

In this group of cases the resectability figure was 73 per cent. To improve the horizon of operability and to remove every cancer of the colon possible, one must accept border line cases. Surgical removal of 3 out of 4 cancers of the colon accepts this principle as a necessity. The mortality figures in the right colon of 17.5 per cent are too high. On two former occasions I have reported mortality figures of less than 12 per cent for a series of right colonic cancers removed surgically. The latter figures should be accomplished in the hands of most surgeons without difficulty and will be possible, I think, if the graded procedure is accepted in all cases of cancer which are not freely movable or are complicated by local or general conditions. Certainly in order to do a one stage procedure one must select only the most favorable cases for resection. The mortality figures in the left colon were 10.2 per cent, with a resectability figure of 72 per cent.

Table II is an epitome of the entire group.

TABLE II.—OPERATIONS FOR CANCER OF THE RIGHT AND LEFT COLON

100 Males	78 Females
Total cases right and left colon, diagnosed	178
Total cases right and left colon, treated	170
Total operations	212
Total mortality, per cent	11.7

Many maneuvers permit a wide range in selecting a type of operation for radical extirpation for cancer of the colon and rectum. The cardinal principle of wide removal of the growth and the tissues in immediate juxtaposition to it, as well as lymph gland bearing tissues situated more distantly is, of course, the ideal sought. Any type of operative procedure which gives a high percentage of ultimate cures must take into consideration the lymphatic system's relationship to metastasis.

The brilliant works of David and Gilchrist, of Gabriel, Bussey, and Dukes, and of Coller, Kay, and MacIntyre, are monuments to industry for they show beyond peradventure that

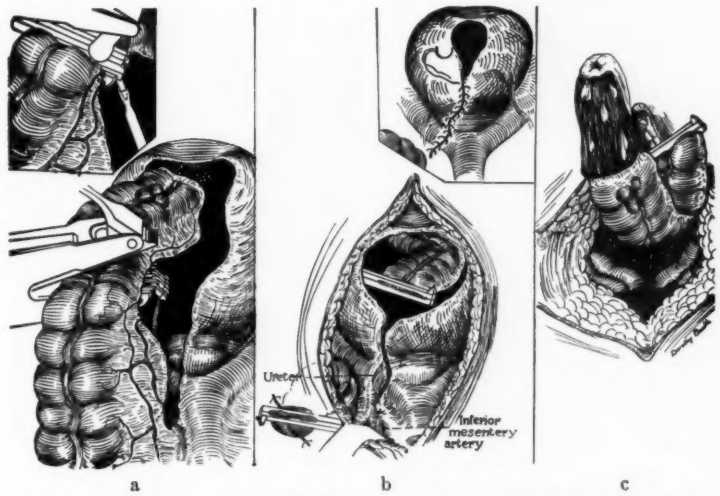


Fig. 3. The steps in a combined abdominoperineal resection of the rectum in one stage. a, Shows mobilization of the growth after ligation of the blood supply is completed. The pelvic dissection is shown completed and the Cope-DeMartel clamp applied. b, Shows the bowel and growth dropped back into the pelvis, a new floor being formed and the single barrel colostomy made through a stab wound in the groin. c, The beginning of the posterior dissection. The rectum is mobilized up to the peritoneal fold and is then removed by this posterior approach.

the more glands one inspects the more metastases one finds. Coller and his associates found that 60.8 per cent of all resections of the colon showed glandular involvement if a large number of glands were studied. Isolating an average of 52 glands per specimen, it was found that 59.4 per cent nodes showed malignant involvement, and 41.4 per cent were without metastases. Here again they emphasized a paradox which has long been recognized, namely, that a higher percentage of cancers of the right colon show metastasis than do cancers of the left colon. Actually 62.5 per cent of the cancers of the right colon in their series showed metastasis in comparison with 60 per cent of those of the left colon. Despite these figures more individuals who undergo operations for cancer of the right colon survive at the end of a given period than do those undergoing operations for cancer of the left colon. An explanation of this fact is not forthcoming, but statistics are definite on it.

David and Gilchrist, in 1938, had a similar experience in dealing with cancer of the rectum. They found that in 68 per cent of rectal cancers glandular metastasis could be demonstrated by a careful examination of a large number of glands. This work is supported by statistics from St. Mark's Hospital in London and has been buttressed by all investigators who have taken the pains to make examinations of large numbers of glands. It established beyond any question proof that widespread resection of the mesentery is necessary; consequently, a most important decision in choosing an operation for cancer of the colon comes, first, between graded and single stage procedures, and second, between immediate anastomosis and delayed union. There are surgeons who glibly assert that colonic resection should always be done in one stage, or on the other hand, two stages. Obviously there is a middle ground which is predicated upon the ability of the patient to undergo formidable resection in one operation, and the question of whether or not his condition will be advantageously treated by multiple procedures. Local conditions such as fixation, infection, and obstruction, and general conditions, such as age, obesity, and coexisting debilitating disease, decide the selection in the average

TABLE III.—CANCER OF THE RECTUM AND RECTOSIGMOID

275 Cases diagnosed
262 Cases treated

175 Males	100 Females
Diagnosis made	275
Treatment given	262
Males	175
Females	100

Disposition of cases	Cases	Deaths	Per cent Mortality
One stage combined abdominoperineal resection	136	9	6.6
Two stage combined	7	0	
Colostomy and posterior resection	49	4	8
Posterior resection	1	0	
Radium	4	0	
Palliative Procedures			
Colostomy alone or with exploration	52	8	15.3
Exploration alone	10	0	
Cecostomy	3	1	
	262	22	

TABLE IV.—OPERATIONS FOR CANCER OF THE RECTUM AND RECTOSIGMOID

	Cases	Deaths	Per cent Mortality
One stage combined abdominoperineal resection	136	9	6.6
Colostomy and posterior resection	49	4	8
Posterior resection	1	0	
Colostomy alone or with exploration	52	8	15.3
Exploration alone	10	0	
Two stage resection (Rankin)	7	0	
Cecostomy (acute obstruction due to cancer)	3	1	
	258	22	8.5

258 cases—(320 operations)
193 resections — Resectability...74.8 per cent
193 resections
136 one stage combined abdominoperineal resection — Applicability...70.4 per cent

case. The final and ultimate decision will come only on exploration and individualization of cases at the operating table. Inevitably one must fit the operation to the patient and not the patient to the operation and such a program demands familiarity with many types of technical procedures.

There were 275 cases of cancer of the rectum, 258 of which were operated upon; 4 were treated by radium, and 13 refused operation or went elsewhere. In this group there were 175 males and 100 females.

In selecting an operation for cancer of the rectum, it is my confirmed opinion that there are few cases in which it is desirable to ignore the necessity of a colostomy as one of the steps of the operation. There are many reasons if one needs more evidence than the number of involved glands found in resected specimens, why colostomy should be routinely employed. Certainly the burden of proof rests on those who would salvage the sphincteric mechanism to show that a comparable percentage of patients will be alive and free from disease in a given period of years. My own experience with the sphincter saving operations has been paralleled by that of many colleagues and may be summed up briefly in the statement that they usually are followed by recurrence, fistula formation, or stricture. It must be an extremely small percentage of cases of rectal cancer of low grade which have not metastasized and which are located favorably for local excision and segmental resection. This group in comparison to the whole is relatively insignificant.

Table III indicates the distribution of the rectal cancer cases treated in this series during the designated period. It will be noted that 13 cases were not treated by me. Of the group of 275, three of these were sent to me by colleagues for consultation and subsequently were operated upon by these surgeons. A combined abdominoperineal resection of the rectum was successfully performed in each case. The 10 other patients went elsewhere for advice and treatment for various reasons. A few of these people refused operation because of my insistence upon colostomy as a part of the procedure. It has been my plan to hold fast to this principle. Occasionally patients do refuse.

Table IV shows the type of operation, mortality and resectability percentages as well as the applicability of the one stage operation in this series.

It will be noted that the trend in this series was definitely toward the one stage combined abdominoperineal resection of Miles. Over a period of 15 years, I have found myself changing from a graded procedure in treating cancer of the rectum to a single stage opera-

tion wherever it is feasible . . . the reverse of practice in treating cancer of the colon. The advantages and disadvantages of a one stage combined operation are well known. A consideration of end-results leaves few arguments necessary to establish the desirability of this radical one stage operation, but if further arguments were needed, the splendid work of David and Gilchrist and our English colleagues should convince the most stubborn that radical resection of a large portion of the mesentery of the sigmoid is definitely essential.

My own operation is useful only occasionally. When it is noted that I have performed it only 7 times in 262 operations its utility in a very small field is definitely established. Mummery's operation, while less radical than Miles' is a very useful procedure and should be applied to the less sturdy risks and to those individuals who for one reason or another are unable to withstand a formidable one stage operation.

The resectability rate in this series was 74.8 per cent. Of 258 patients operated upon, 193 were subjected to resection of one kind or another. The applicability of the one stage resection to the whole group was 70.4 per cent.

This seems to indicate that with proper preliminary preparation one may apply the one stage combined abdominoperineal resection of the rectum not routinely, but at least with great frequency in any given series. The mortality statistics show that the one stage procedure may be accomplished with a death rate comparable to that of other procedures. In 136 operations there were 9 deaths; a mortality of 6.6 per cent. This compares favorably with the group operated upon by the two stage procedure; 49 Mummery operations being performed with 4 deaths; a mortality of 8 per cent. The total mortality of the whole group was 8.5 per cent, with a resectability rate of 74.8 per cent.

Mortality statistics and curability figures are inextricably bound together and are influenced by many factors. Operability varies in the hands of different surgeons because of many circumstances peculiar to the surgeon and the case. Suffice it to say that it is a well recognized axiom that every effort should be made to extend operability curves which so vitally influence end-result percentages. Standardization of preoperative and postoperative measures as well as flexibility of the operative phase of the attack will no doubt still further reduce hospital casualties, morbidity figures, and thereby enhance the satisfactory ultimate outcome. It is widely conceded that prognosis following successful radical extirpative measures for cancer of the lower gastrointestinal tract is satisfactory by present day standards. Nevertheless, the ultimate goal is far from reached and continued effort is essential to amplify efforts to combat successfully this modern scourge by surgical methods.

THE TREATMENT OF PATIENTS WITH SEVERE BURNS

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THE surgical principles involved in the treatment of burns are often forgotten, sometimes ignored, in the constant effort to find new and improved methods of treatment. These principles can be expressed very simply by stating the objectives of treatment. They are:

1. To prevent and combat shock.
2. To convert the open contaminated wound into a clean wound.
3. To cover the open wound by the simplest possible dressing that (a) protects it from the constant danger of reinfection; (b) does not fix or destroy any part of the skin or subcutaneous tissue which remains viable when the patient is first seen; (c) provides for drainage of the serum that exudes from the burned surface until it is checked by pressure or the normal process of coagulation; (d) exerts a uniform moderate pressure over the burned area; and (e) can be easily removed if infection develops underneath the dressing or if the burn involves the whole thickness of the skin.
4. To keep the injured part at rest.
5. To secure healing in the minimum period of time and with minimum loss of function.

If these principles are sound they apply whatever the extent, the location, or the severity of the burn, and the effort to classify burns into first, second and third degree, or to distinguish between the treatment of burns of the trunk and burns of the face and extremities may only divert attention from essential factors in the treatment.

So much controversy has arisen and so many conflicting ideas have been expressed concerning the local treatment of burns that we wish to postpone for the moment the discussion of the problem of shock and consider first the principles involved in the local care of the burned area.

From the Division of Surgery, Northwestern University Medical School, and the Children's Surgical Ward of the Cook County Hospital.
Read before the Chicago Surgical Society February 6, 1942.

CONVERSION OF THE OPEN CONTAMINATED WOUND INTO A CLEAN WOUND

This principle, often completely ignored in discussions of burns, is of primary importance. To cover a burned area with chemical or coagulating solutions without first using every effort to transform it into a clean wound seems to us an inexcusable disregard of fundamental surgical principles.

If the burned patient is still clothed, adherent and burned clothing is best soaked off in a tub of clean water maintained at a temperature of 100 degrees F. in a room reserved and equipped for the treatment of burned patients. The process is rendered almost painless by giving the patient an adequate dose of morphine immediately after admission. We have not used other analgesics or anesthetics even in children with very extensive burns. The room is kept at a temperature of 80 degrees F., and opening of the doors while treatment is in progress is avoided to prevent currents of air from blowing through the room.

With the burned area free from clothing and débris that can be removed by soaking and the surrounding uninvolved area cleansed with soap and water the patient is lifted upon a table covered with a sterile sheet and cleansing of the burned area begun.

To transform an extensive and contaminated raw surface into a surgically clean wound, and without adding further injury and bacterial contamination requires time, patience, gentleness, plenty of soap suds, and continuous irrigation with sterile water of a temperature of 100 degrees F. Obviously the surgeon, his assistants, and the patient must be masked. The surgeon and his assistant wear sterile gowns and gloves. Every effort is made to carry out the same careful technique that one would carry out in performing an abdominal operation.

Grease or ointment which may have been applied over the burned surface can usually

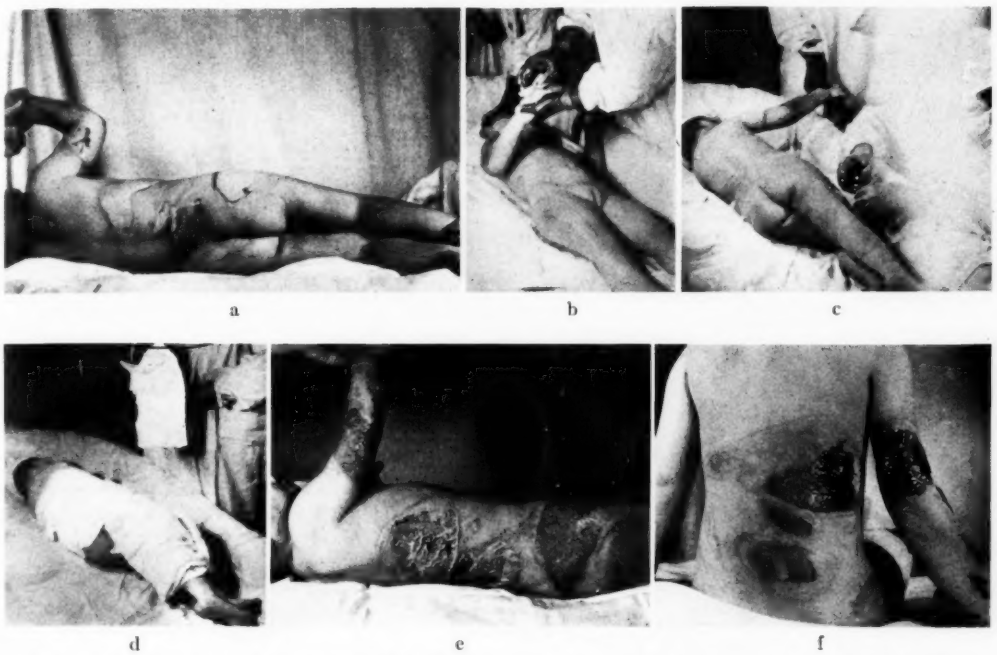


Fig. 1. Extensive burn with large areas of whole thickness destruction. a, On admission; b, cleansing of burned surfaces; c, excision of necrotic tissue; d, application of pressure dressing; e, after removal of primary dressing, 13 days after admission; f, appearance of burned areas 20 days after admission, just before application of skin grafts.

be washed off with soap suds. If not, a fat solvent such as benzene is used.[1] The actual cleansing is accomplished with large "wash cloths" of soft sterile cotton, plain white soap, and sterile water. Green soap, gauze, scrubbing brushes are avoided as causing unnecessary trauma. Blisters are opened with sterile scissors; shreds of epithelium and skin that can be lifted away with forceps are removed. No excision that might cause bleeding is made.

DRESSING OF THE WOUND

With the injured surface cleansed as completely as possible it is smoothly covered with a few layers of fine meshed gauze impregnated with petrolatum. Such gauze is easily prepared in strips 3 inches wide and 12 inches long and sterilized in a porcelain basin provided with a well fitting cover. This dressing does not adhere to the raw surface as does a coagulant crust, it does not fix tissue, and it still permits drainage of serum and exudate into the dressings outside it.

Over the petrolatum gauze are laid a half dozen layers of flat dry sterile gauze, over this a mass of gauze fluff and over the fluff mechanics' waste or sea sponges so as to provide under the retaining bandage a resilient covering that produces an even pressure over the injured extremity or the burned surface but does not cause constriction.

The dressing and compressing sponges are held in place preferably with an elastic bandage such as stockinet. This is particularly advantageous if the burn involves the trunk.

The advantages of pressure over an injured surface have been well stated by Blair:

"The application of most any dressing produces pressure, but he who employs this pressure in a selective, purposeful manner will get bigger returns than he who applies it incidentally or even as a matter of routine.

[1] Johnston of Detroit has found lard an excellent medium for removing oil and grease. Any lard remaining on the skin can be washed away with soap and water.

Fig. 2. Extensive burn with loss of partial thickness of skin. a, On admission; b, after soap and water cleansing and excision of devitalized tissue; c, on discharge from hospital, 14 days after admission; burned area healed.

"There are chiefly four basic things to be gained by the use of properly applied mechanical pressure to wounds:

"The elimination of dead spaces.

"The control of oozing.

"The limitation of venous and lymph stasis.

"Limitation of the amount of plastic material that pours into the wound."

The elimination of dead spaces into which constant oozing can take place and the limitation of exudation from the surface of a wound *and into the subcutaneous tissues* are important objectives in wound treatment which are too often completely ignored. The surgeon who sees blood escaping rapidly from an open wound instinctively applies pressure to stop the bleeding and conserve vital body fluid. By some curious inconsistency if we *cannot see it*, we may ignore the subcutaneous bleeding that goes on just as definitely after the subcutaneous rupture of blood vessels and continues until it is arrested either by coagulation or by actual compression of the injured blood vessels by the tensed body tissues.

If this subcutaneous bleeding is the "white hemorrhage" that goes on in tissues injured by a flame or scalding water, it needs to be arrested just as promptly as if the blood were escaping from a torn blood vessel. It can be arrested, and body fluid saved by the application of pressure over the injured area.

REST FOR THE INJURED PART

The importance of rest for injured tissues has been emphasized with increasing frequency since war and its accompanying disasters have again focused attention on the treatment of severe and multiple compound injuries. The "magic of the plaster cast" has proved to be due in large part to the "uninterrupted and enforced rest" of injured tissues which was so important a principle in the creed of Hugh Owen Thomas. It is as important and essential a part in the treatment of severe burns and of other soft tissue injuries as it is in the care of compound fractures.

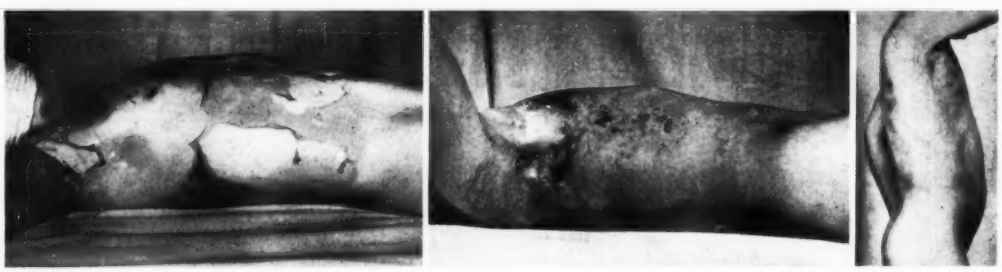


Fig. 3. Extensive burn with limited areas of whole thickness destruction. a, On admission; b, after removal of primary dressing 12 days later; c, on discharge from hospital, 69 days after admission. Healing of areas of whole thickness loss could have been hastened by early skin grafting.

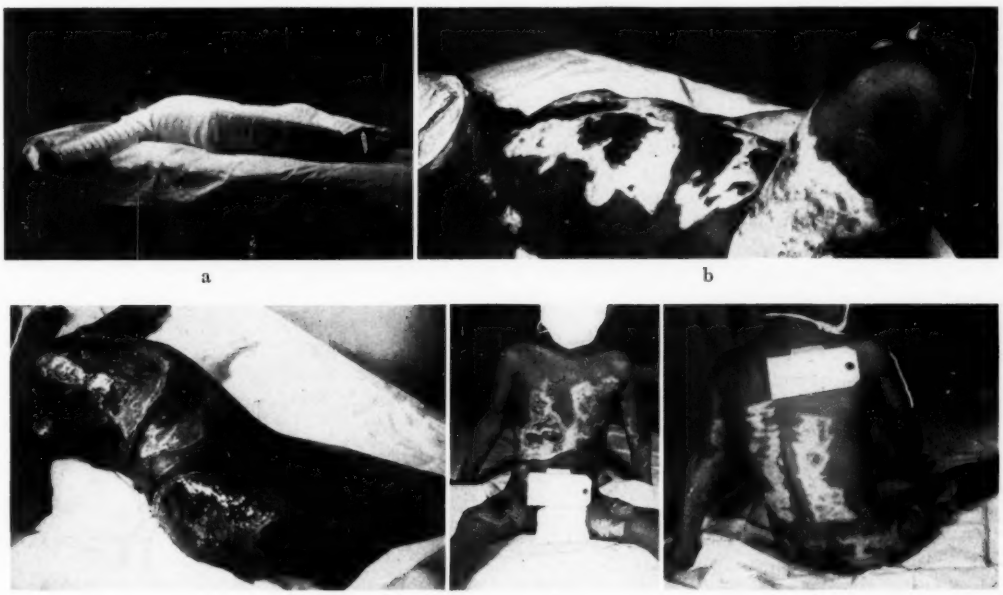
a b c d

Fig. 4. Severe burn with extensive destruction of covering tissues. a, On admission; b, after removal of primary dressing; c, 13 days later; d, appearance 33 days after admission, shortly before skin grafts were applied.

HEALING OF THE BURNED SURFACE

The mechanism of healing after partial or complete destruction of covering skin is sometimes forgotten in the face of the constant emphasis on new methods of treatment which are stressed so strongly by lay writers in *Hygeia*, the *Reader's Digest*, and other nonscientific journals.

If there has been loss of only a partial thickness of the skin, in other words, if there still remain epithelial elements—sweat glands and hair follicles—of the deeper portion of the corium rapid re-formation of the covering epithelium takes place: (1) if the remaining epithelial elements are not fixed and rendered inert by a coagulating agent; (2) if no infec-



a b c d e

Fig. 5. Severe burn with extensive area of whole thickness loss. a, After application of pressure dressing and immobilization with splints; b, after removal of primary dressing, 12 days later; c, appearance 23 days after admission; d, appearance on discharge, 53 days after admission; e, appearance on discharge showing some of grafted areas and, on dorsum of trunk, healing of areas from which grafts were taken.

Fig. 6a.

Fig. 6. Severe burn involving 44 per cent of body surface. This patient received 8 plasma transfusions of 500 c.c. each during the first week, and 2 blood transfusions of 500 c.c. each during the second week. a, Patient on fifth day under oxygen tent, with burned areas covered with compression dressing. Plasma being given through vein in leg; b, c, after removal of primary dressing on fifteenth day; d, e, just before application of skin grafts on thirty-sixth day after admission; raw surfaces are being dressed with moist fine-meshed gauze, over which pressure dressing is maintained; f, 42 days after admission, 6 days after application of skin grafts; g, 15 days later, 57 days after admission.

tion supervenes; (3) if regenerating epithelium is not torn away and destroyed by careless or frequent or too early removal of the protective dressing.

In cases with loss of partial thickness complete regeneration of epithelium takes place in 10, 12, or 14 days; and healing of the burned area should be complete when the primary dressing is first removed at the end of 12 or 14 days.

If the burn has resulted in a whole thickness loss of skin no *dressing* can bring about regeneration of epithelium. Re-formation of covering skin can come only by ingrowth from the periphery or as a result of skin grafting. To await spontaneous healing if the denuded surface is more than 2 or 3 square inches in area is only to delay recovery. Moreover, to wait indefinitely for spontaneous separation of a coagulant crust or of the charred adherent tissue that represents the destroyed surface covering causes serious and unnecessary delay in healing. Cleanly surgical care after the removal of the primary dressing, subsequent dressings at regular intervals of 24 or 48 hours with removal of any adherent tissue that can be cut away without causing pain or bleeding, and the use of dressings saturated with Dakin's solution, all help to hasten separation of the covering tissue destroyed by the original injury, and help to counteract the infection that tends to develop in the presence of an open wound and necrotic tissue.

During this stage of treatment our primary objective is to secure a covering of healthy granulations as soon as possible so that skin grafts can be laid over the raw surface. Here again a number of details in treatment are of great importance. They are: (1) cleanly

Fig. 6b.

Fig. 6c.

Fig. 6d.

Fig. 6e.

Fig. 6f.

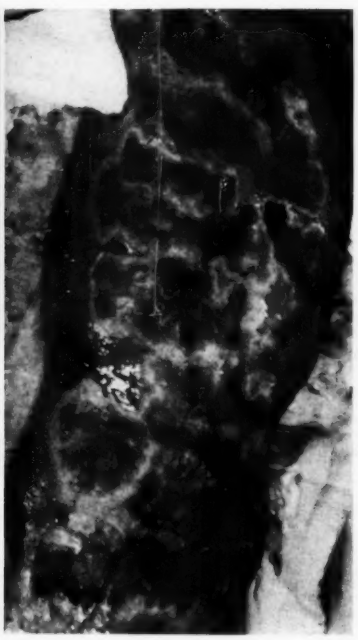
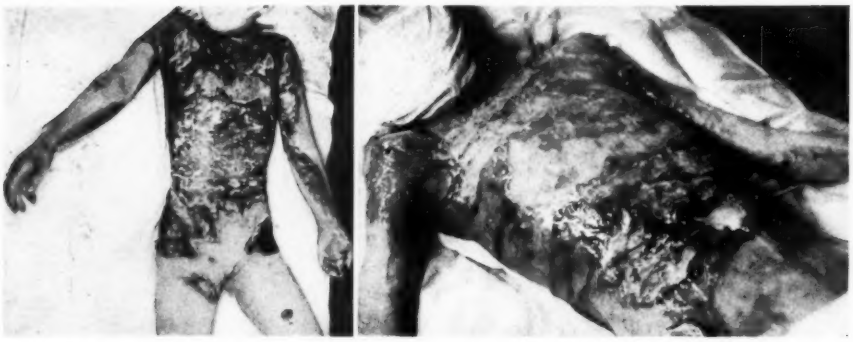


Fig. 6g.

(*Legend on opposite page*)

surgical care; (2) avoidance of trauma; (3) the application of at least one layer of very fine meshed gauze directly over the raw surface so that granulations cannot readily become enmeshed in the gauze; (4) over the fine meshed gauze moist sterile gauze to favor drainage; (5) over the moist gauze sufficient sterile dry gauze to prevent contamination from without; and (6) the use of pressure to aid the return circulation and prevent the



a b

Fig. 7. Extensive burned area coagulated with tannic acid applied by members of Fire Department. Severe infection developed under the crusts, and to remove crusts and necrotic tissue, control infection, and secure healing required 6 months' time. a, On admission; b, appearance 4 days after application of skin grafts over large raw surfaces.

congestion that results from the temporary loss of the normal outer retaining wall against which the venous channels can be compressed.

As soon as a covering of healthy granulations is secured and the patient's condition permits, the raw surface should be covered as completely as possible with grafts of intermediate thickness. The sooner this can be accomplished the sooner will recovery be achieved and the less will be the disability and the contracture that steadily increase as long as a raw surface remains unhealed.

COMPLICATIONS FOLLOWING BURNS

The complications resulting from burns have aroused almost as much controversy as the question of local treatment. Many papers have been written on the problem of burn shock, toxemia, and infection. Without wishing to oversimplify the problem we would simply state our belief that the initial shock is due to pain, fright, and overexertion; and is often followed very quickly by secondary shock resulting from loss and shifting of body fluids; that unequivocal evidence has not yet been produced to show that acute toxemia results from the effect of a circulating toxin formed by autolysis of the burned tissue (Wilson); thirdly, that in the cases under our observation infection developing after a burn has been a feared and serious complication only in patients who were admitted to the hospital 24 or 48 hours after the injury and whose primary treatment often consisted of the application of ointments of some type.

Shock. Most observers are agreed that primary shock can be severe and is not necessarily dependent on the extent of the burned area. Fright; frantic efforts to avoid injury or to escape from a burning building or from underneath crushing wreckage; sudden and powerful muscular exertion far beyond that normally employed—all can lead to sudden collapse that may appear unexplainable to the observer who sees only an injury of limited extent and severity. For this primary shock morphine is the most effective aid, and in our judgment the morphine need not be supplemented by a general anesthetic. It is of significance to us that the workers who have stressed the theory that a burn toxin is responsible for early death in fatal cases have persistently used anesthetics, including ether, during the initial process of cleansing and tanning.

Many observers are agreed that secondary shock is due to loss of body fluid from the burned surface and, still more important, *loss of fluid into the subcutaneous tissues.* The latter is comparable to the bleeding that occurs into a crushed limb; and although a great deal of effort has been expended to determine how rapidly the loss can take place, how large a percentage of the available body fluid can escape into the subcutaneous tissues, and

what the effect of that loss is on blood volume, blood concentration and blood pressure (1, 3, 8) little emphasis has been laid on the importance of arresting the "white hemorrhage" and preventing the shock producing loss of body fluid.

It is to prevent this loss that we have emphasized the importance of pressure applied over the entire burned area or around the affected limb as soon as the open contaminated wound has been converted into a clean wound; and, after the application of the pressure dressing, as complete immobilization of the injured area as it is possible to secure.

In spite of every effort to prevent loss of body fluids in patients seen late and in those with extensive burns the loss may be sufficiently great to lead to shock and collapse. In such cases prompt replacement constitutes a life saving procedure. Many workers have made helpful contributions to the solution of this problem, and without discussing in detail the studies of Harkins, McClure, and their associates, of Scudder, of Trusler and his associates, of Rhoads, Wolff and Lee we would simply say that we agree with the statement that "plasma transfusion is the most logical type of replacement therapy and that it has given the best clinical results" (14).

To estimate the extent of fluid loss and the need for replacement during the early and critical stage of treatment the hematocrit reading is an easily obtained and dependable guide. The determination made immediately after admission of a patient with a severe burn can be used as a standard against which to check subsequent readings. Significant changes in blood volume may not be reflected immediately in the clinical symptoms, but a slow steady increase in the hematocrit level indicates that hemoconcentration is taking place and that the loss into the tissues should be compensated for by administration of plasma.

In cases seen late thirst, restlessness, and a rapid pulse rate are constant and important signs of fluid loss and indicate the need for prompt administration of plasma in adequate amounts. To give transfusions of whole blood in such cases, as has been frequently pointed out, may add to hemoglobin concentration; and to give water alone in large amounts, as Trusler and his associates have emphasized, may lead to "water intoxication."

The administration of oxygen, particularly in patients with burns of the face and chest, is a valuable adjunct to treatment. In patients with burns of the face and chest the inhalation of irritating gases and the resulting congestion and inflammation of the upper respiratory passages may add another handicap and contribute to the development of anoxemia. We have given oxygen as part of the routine treatment in patients with burns about the face and chest and have thought it to be of definite benefit.

Toxemia. The formation of a burn toxin as the result of destruction of the superficial body tissues has been considered by many workers to be the determining factor in causing death in patients with severe burns. Wilson and Stewart and their associates at the Edinburgh Royal Infirmary, particularly, have stressed the frequency with which the picture of acute toxemia develops in from 6 to 50 hours after injury in those cases which go on to a fatal termination. They have emphasized the frequent occurrence of jaundice in these cases and the degeneration and necrosis of the liver seen after death. They have injected into healthy animals "edema fluid" from the subcutaneous tissues of burned animals with resulting fatal toxemia and pathological changes similar to those seen after death from severe burns.

We have no definite evidence either to support or refute the theory that a burn toxin results from destruction of superficial body tissues. The few cases we have observed after death have shown acute degenerative changes in all the parenchymatous organs. The pathological change has not been limited to the liver, nor have we seen the extensive liver changes described by Wilson and his associates.

We would like to point out again that the fatal cases cited by Wilson all received a general anesthetic shortly after the injury. To give ether to a patient with impending shock, particularly a child, seems to us a dangerous procedure, which may well predispose to intensification of shock, the hemocon-

centration stressed by Underhill, and the resulting anoxemia which has been stressed by McClure and others as a grave threat to the injured patient.

Infection. For years past infection has hung over the head of the burned patient like a veritable sword of Damocles, threatening life and destroying tissue. No one who has had the responsibility of caring for severely burned patients can erase from his mind the picture of the anxious, feverish child with an extensive, severely infected raw surface, anticipating with constant dread the daily ordeal of change of dressings.

The doctor who asked, "Is it true that every patient with an extensive burn eventually develops a blood stream infection?" was simply voicing what has been more or less generally accepted as the inevitable accompaniment of an extensive burn.

To some the statement that infection is the result of careless or unthinking treatment may sound as heretical as Holmes' indictment of the medical profession concerning the responsibility for puerperal infection. Holmes did not know, what has since been demonstrated, that of almost equal importance with infected hands and contaminated clothing as sources of contagion are the mouth and nose of carriers of virulent streptococci and staphylococci. Hare's admirable studies have brought laboratory explanation of the often repeated clinical observation that in most instances the greatest menace to the patient is not the object that causes the open wound, not infection that may have been present on the patient's clothing or on his skin, but infection that comes from the open mouth and uncovered nose of excited and voluble bystanders, of enthusiastic first aid workers, too often of the doctor and nurse who are caring for the patient without masking themselves and without making certain that their hands and their surgical instruments are free from pathogenic bacteria.

When we recall the fact, so forcefully stressed in a recent editorial by Mason, that a burn is in all its essentials a large open wound, and when we consider the elaborate precautions every surgeon constantly takes in the operating room to prevent infection of even a small open wound we cannot but wonder at the inconsistency of failing to take the same precautions in preventing infection of a wound far more extensive than the largest wounds which the surgeon ordinarily sees in the operating room.

If one were to ask the junior medical student why the surgeon and everyone else in the operating room is carefully capped and masked he would have a ready answer. If we were to ask him why in the initial treatment of a patient with an extensive burn, or during the change of dressings in the days following injury such precautions are seldom taken what would he say?

To express it as concisely as possible it is our belief: (1) that the most important source of infection of a burned surface is from the open mouth and uncovered nose of individuals working over the injured patient; (2) that infection can be prevented in almost every case if the patient is seen promptly after injury and if he has not received extensive or prolonged "first aid" treatment; (3) that the simplest and safest method of converting an open contaminated wound into a clean wound is by gentle, thorough cleansing with plain white soap and sterile water applied with gloved hands under eyes that are alert and mouth and nose that are carefully masked; and (4) that it is neither logical or wise to substitute for a safe and tested method an elaborate time consuming procedure which involves the use of powerful chemicals concerning whose possibilities for harm we are still in doubt.[1]

To say that the application of a coagulant over a burned surface is not the ideal or most desirable type of dressing in no way detracts from Davidson's splendid contribution to the problem of burn treatment. Davidson taught us two important facts: that if a burned surface is covered promptly with an occlusive dressing the constant danger of infection of the large open wound is eliminated; and secondly, that the prompt application of a dressing which checks the constant loss of serum from the burned surface diminishes the loss of vital blood plasma.

[1]Cases of sulfadiazine poisoning and a fatality resulting from the application of sulfadiazine in triethanolamine as recommended by Pickrell, have been reported.

MORTALITY RECORD

	Method of treatment	No. of cases	No. of deaths	Percentage of mortality
1934–1936	Tannic acid.....	395	39	10
1937 (10 mos.)	Tannic acid and silver nitrate (Hedin).....	82	6	7.3
1939	Nonadherent dressing with pressure....	137	8	5.8
1940	.....	164	6	3.65
1941	.....	185	5	2.7

If we can accomplish these objectives and others of equal importance by a simpler method than the application of tannic acid it means that we are making progress, and not clinging to an outmoded method—even though that method represented a definite advance fifteen years ago.

Under a régime such as that outlined above the results obtained in patients with severe burns in the Children's Surgical Ward of the Cook County Hospital have steadily improved. The accompanying table indicates the mortality record only.

As evidence of the severity of the injuries treated is the fact that of the 19 patients who died as a result of burns in the years 1939–1941, 10 died during the first 24 hours, and 3 during the second 24 hours after admission. Of 6 patients who died later, 3 were transferred from other hospitals, and in these cases the control of infection was an outstanding problem.

In addition to the cases of severe burns were many patients who were not admitted to the hospital or remained in the hospital less than 24 hours. These patients were treated by the same method, and in this group of cases there were no deaths.

Other workers have obtained equally satisfactory results with the method of treatment described. Siler of Cincinnati showed a colored motion picture at Boston in November, 1941, which graphically illustrated the essential details of treatment—wound cleansing, the application of a nonadherent dressing, compression, and continued rest, and which showed the excellent results obtained by the application of these principles to the treatment of burns at the Cincinnati General Hospital.

Space does not permit extended discussion of the improved results that have followed as far as time expended for nursing care, time required to prepare the raw surfaces for skin grafting, and duration of hospital stay are concerned. Nor can one dismiss the subject without emphasizing the constant cooperation on the part of the nursing and resident staff that is essential for good results. The entire nursing staff of the Children's Surgical Ward, the surgical residents,—Lt. Clayton Brock now at Camp Shelby, Mississippi, Lt. William Requarth, now with Submarine Squadron 4 at Pearl Harbor, and Drs. Frederick Leeseman and W. A. Yemm of the present resident staff—have all given their constant, whole hearted co-operation to secure the best possible treatment for these seriously injured patients. Without their help it would have been quite impossible to secure the results that have been obtained.

A final word should be added concerning the management of burned patients under emergency conditions. Some of you will say that one cannot possibly carry out the treatment suggested under war conditions or when numerous casualties confront the surgeon.

It is our belief that under such conditions, as well as with patients who come to the surgeon late, or who have received prolonged "first aid" treatment under unfavorable conditions, the sulfonamides can be used to great advantage. An ointment containing a sulfonamide, for example, such as has been successfully used by Allen, Owens, and Dragstedt, can be rapidly spread over the burned surface, covered with a sterile dressing and a compression bandage. The ointment should be applied with a clean spatula and by a masked orderly or nurse. In other words, even under emergency conditions there can be no excuse for not protecting the open wound from contamination with organisms from uncovered mouths and noses.

Patients so treated could be transported to field hospital or casualty clearing station where the treatment outlined in the preceding pages would be carried out. It might well be emphasized again that after cleansing is completed and a pressure dressing applied the patient is left undisturbed for from 10 to 14 days unless some complication arises. If transportation of the patient becomes neces-

sary it can be accomplished with minimum difficulty and without change or interruption of treatment. In other words, the simplicity of both the initial treatment and the post-operative care should commend such a method if it is based on sound surgical principles.

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INVERT SUGAR AS A SUBSTITUTE FOR GLUCOSE IN INTRAVENOUS THERAPY

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INABILITY to secure glucose because of blockade and interruption of commerce by the war resulted in the trial of invert sugar for intravenous therapy, with satisfactory results. The following report on the method of preparation of invert sugar solutions from ordinary cane sugar and the results observed will be of especial interest wherever hospitals are isolated from their usual sources of supply.

During the last world war (1914–1918) Mayer and Guerbet used invert sugar prepared from sucrose for intravenous injections, because of difficulty in obtaining pure glucose, which at that time was frequently contaminated with lead and arsenic. They stated that the physiological and therapeutic actions of the invert sugar preparation were identical with those of glucose. Even though glucose of satisfactory quality was available soon after the war, the use of invert sugar rather than glucose continued in Germany at least up to 1930 (9). Invert sugar solutions for intravenous use were placed on the market in Germany under the proprietary name of "calorose" (10, 12), and methods for making nonproprietary substitutes for "calorose" were published by Danish pharmacists in 1930 (7). Cousin and Fagon in 1937, finding difficulty in securing pure glucose in the French colonies, turned to the use of invert sugar, using a modified form of the method of Mayer and Guerbet. In the American literature we have found no references to the use of invert sugar for therapeutic purposes.

The earlier methods recommended for the preparation of invert sugar solutions for parenteral use depended upon the hydrolysis of sucrose with phosphoric acid (3) with subsequent removal of phosphate as the calcium salt by interaction with calcium carbonate, or with tartaric (12) or hydrochloric acid (7), the acids being subsequently neutralized with sodium carbonate. Hansen, Shou, and Tonnesen used small amounts of hydrochloric acid as the hydrolytic agent with no attempt at neutralization, producing solutions with a pH of about 3.

We have adopted a method recommended for the preparation of invert sugar solutions for use in the so called Böeseken titration (1). In this procedure a hot concentrated solution of sucrose is hydrolyzed rapidly with hydrochloric acid, which is then exactly neutralized with an equivalent amount of sodium hydroxide. The resulting solution diluted to a concentration of 5 per cent (calculated as hexose) is a clear, colorless liquid with a pH between 4.5 and 6.0, containing not more than 0.01 per cent of sodium chloride and 0.05 per cent of unhydrolyzed sucrose.

REAGENTS

Freshly distilled water (not over 12 hours old) should be used in the preparation of all reagents, as well as for solution of the invert sugar. It is well known that reactions following intravenous injections of saline or glucose are most frequently due to the use of distilled water in which "pyrogenic" bacteria have grown.

Hydrochloric acid. Prepare a solution approximately normal in strength by a 1 to 10 dilution of concentrated (38 per cent) hydrochloric acid.

Sodium hydroxide. It is essential that this be of exactly the same normality as the hydrochloric acid. Adjust the concentration of a 5 per cent solution until 25 cubic centimeters of the hydrochloric acid solution are exactly neutralized by the same volume of the sodium hydroxide solution. Keep in a paraffined bottle provided with a siphon and a soda-lime tube to prevent contamination with silica and carbon dioxide.

From the Biochemical Research Foundation, Newark, Delaware, and the Departments of Biological Chemistry and of Pharmacy, American University of Beirut, Beirut, Republic of Lebanon.

Indicator. For adjustment of hydrogen-ion concentration a convenient indicator is made by mixing equal parts of methyl orange (0.1 per cent in 50 per cent alcohol) and brom-cresol-purple (0.04 per cent in water). This indicator, when used in the proportion of 4 drops per 5 cubic centimeters of solution, gives a yellow color between pH 4.4 and 5.8 (a range suitable for intravenous injection). Below pH 4.4 the indicator gives a reddish color, and above 7.0 a purplish color.

Hydrogen-ion concentration standards. Although the hydrogen-ion concentration may be adjusted to within the proper range by merely observing the color given by the indicator as herein noted, it is advantageous to have known standards for reference. Nine standards between pH 4.0 and 7.2, with intervals of 0.4 are sufficient. Directions for the preparation of these may be found in any biochemical manual (e.g., Cole). Measure 5 cubic centimeters of each standard into test tubes and add to each 4 drops of the indicator.

METHOD OF PREPARATION OF INVERT SUGAR SOLUTION

Twenty liters of sterile invert sugar solution may be prepared by the following procedure. Dissolve 960 grams of sucrose (commercial granulated table sugar) in 300 cubic centimeters of freshly distilled water in a 2 liter Erlenmeyer flask with the aid of heat and with continuous rotation of the flask to avoid caramelization; then bring to the boiling point and boil for a minute or two until clear. With a pipette add exactly 25 cubic centimeters of normal hydrochloric acid and mix the contents of the flask by rotation for 1 minute. Immediately neutralize, while mixing, by adding 500 cubic centimeters of water containing exactly 25 cubic centimeters of the sodium hydroxide solution. The solution should have no more than a light yellow color. The volume is about 1500 cubic centimeters and contains the correct amount of invert sugar to make 20 liters of 5 per cent solution (glucose equivalent).

The stock solution is filtered while still warm through four thicknesses of muslin and then through one thickness of filter paper.

Adjustment of hydrogen-ion concentration. Dilute 3 cubic centimeters of the concentrated preparation to 40 cubic centimeters and mix. To 5 cubic centimeters of this diluted solution add 4 drops of the indicator and compare with the pH standards. If the pH is not within the range 4 to 6.8 (a yellow color indicates 4.4–5.8), titrate 15 cubic centimeters of the concentrated sugar solution with 0.01 normal sodium hydroxide (or hydrochloric acid if it is too alkaline), using 12 drops of indicator, and end the titration at a pH between 4 and 5. To the main solution (1500 cubic centimeters) add a quantity of normal sodium hydroxide (or hydrochloric acid) equal to this titration and mix. Again dilute 3 cubic centimeters to 40 and test the pH.

The stock solution is finally diluted to 20 liters with freshly distilled water within 48 hours, measured into flasks or ampuls and sterilized by autoclaving at 120 degrees C. for 30 minutes. Each flask is inspected for fiber particles before autoclaving and refiltered if necessary.

RESULTS

In a period of 5 months when glucose was not available (November 21, 1940 to April 18, 1941), 2,349 flasks of invert sugar were used for parenteral therapy in the hospitals of the American University of Beirut. Not a single reaction was observed. Previous to this period (November 1, 1939 to October 31, 1940) three reactions occurred in the treatment of 6,180 cases with glucose solutions.

Determinations of total reducing sugar and of levulose in blood were made during and after intravenous injections of invert sugar in normal subjects. The method of Herbert was used for levulose, and that of Shaffer and Somogyi for total reducing sugar, both determinations being carried out on a zinc hydroxide filtrate of the same blood specimen. The results, presented in Table I, show that the rise of blood levulose is much less than that of glucose, the maximum value observed for levulose being 18 milligrams per 100 cubic centimeters at the termination of an infusion of 500 cubic centimeters of 10 per cent invert sugar. Half an hour after the end of the infusion, blood levulose varied from 5 to 9 milligrams per 100 cubic centimeters while total reducing

TABLE I.—TOTAL REDUCING SUGAR AND LEVULOSE IN BLOOD DURING AND AFTER INTRAVENOUS INFUSIONS OF INVERT SUGAR*

Subject	Invert sugar injected	Fasting		During infusion			End of infusion			30 min. after end of infusion		60 min. after end of infusion	
		Reducing sugar	Levulose	Interval†	Reducing sugar	Levulose	Interval†	Reducing sugar	Levulose	Reducing sugar	Levulose	Reducing sugar	Levulose
Bed 11	900 c.c. 5%	72	2.2				35	150	12.7	83	6.3		
Bed 13	900 c.c. 5%	80	2.2				43	200	15.6				
Bed 15	900 c.c. 5%	72	1.6				49	135	13.1				
SEK	900 c.c. 5%	76	3.0				84	100	11.5	70	6.5	68	5.7
JJ	900 c.c. 5%	74	4.1				61	113	9.9	50	5.3	68	4.2
Ham.	900 c.c. 5%	72	2.7				63	117	11.9	52	9.1		
Far.	500 c.c. 10%	66	2.8	27	130	15.3	45	117	17.3	46	5.9	60	4.6
St.	500 c.c. 10%	78	3.6	19	156	14.5	43	180	18.0	62	6.3	56	4.7

*Results expressed in milligrams of sugar per 100 cubic centimeters of blood.
†Number of minutes after beginning the infusion.

sugar was at this time in most cases considerably below the fasting level—a phenomenon also observed when only glucose is injected.

The small amount of unhydrolyzed sucrose in the invert sugar solutions is promptly excreted in the urine. Excretion of reducing sugar varies between 0.6 and 1.1 grams during infusion.

ADVANTAGES OF LEVULOSE

Since invert sugar is half glucose and half levulose, any question regarding justification for its use must involve the intermediary metabolism of the levulose fraction. The review by Deuel as well as other literature supplies ample evidence that levulose is readily converted to glucose and glycogen in the body. It is easily oxidized and causes a prompt rise in the respiratory quotient and in heat production. There is considerable evidence which suggests that levulose is more readily utilized in diabetes mellitus than glucose.

SUMMARY AND CONCLUSIONS

No unfavorable reactions were observed in 2,349 cases following intravenous injection of invert sugar prepared by acid hydrolysis of commercial sucrose. The levulose fraction disappears rapidly from the blood stream, 18 milligrams per 100 cubic centimeters being the highest value observed at the end of an infusion. The results confirm the experience of others that when glucose is not available invert sugar is a satisfactory substitute for intravenous therapy.

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FACTORS INFLUENCING THE END-RESULTS IN CARCINOMA OF THE OVARY

Report of a Series of 138 Patients Treated from 1910 to 1935

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REPORTS on the results of the treatment of ovarian cancer have exhibited a range from below 10 to over 50 per cent of 3 to 5 year cures (Table I). This wide variation is evidently the result of other factors beside the relative merits of therapy as applied by the reporting clinics and must almost certainly be ascribed to different methods of classification or the statistical handling of the case material.

The calculation of any 5 year cure rate is carried out principally to make possible the selection of the best of several methods of therapy or to demonstrate the need of some special procedure, such as postoperative radiation. Statistics on malignant ovarian tumors have failed in this purpose because of the heterogenous character of the group and the differences of opinion as to how it should be reported.

In the present article this problem will be examined in the light of a series of patients treated at the Roosevelt Hospital. At the same time the end-results for these cases will be presented and the effects of radiation therapy reported.

For this work 198 cases of ovarian tumor have been reviewed, including 138 cancers of the ovary and 60 papillary cystadenomas. The series includes all cases belonging to these categories, the patients being admitted to the gynecologic service from 1910 to 1935.

The "absolute" 5 year cure rate among the 138 malignant cases has been placed at 15.2 per cent, when all cases are considered and the lost cases are counted as dead. This figure is approximately that recently reported by Meigs (6) in his review of cases at the Massachusetts General Hospital, but is much lower than the recent figures of Pemberton or of Walter et al.

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The principal factors which may vary the actual end-results, as well as the figures as reported, will now be considered. These are four in number: the gross extent of the disease, the histological type of tumor, the histological grade of the tumor, and the use of radiation therapy.

GROSS EXTENT OF DISEASE (TABLE II)

It is well recognized that the gross extent of the ovarian carcinoma at the time the operation is undertaken is the most important single consideration in prognosis. If one defines an operable case as one in which all cancer was apparently removed, the operability of this series was 31.9 per cent. The known cures in this operable group were 45.5 per cent, while if the many cases untraced for the necessary 5 years, but free of disease when last seen, be excluded, the 5 year cure rate in the operable group becomes 58.8 per cent. The other side of the picture is as gloomy as this is encouraging, for of the 94 cases in which malignant tissue was left behind at the conclusion of the operation or which were recurrent, only 2 have survived the 5 year period.

TYPES OF OVARIAN TUMOR (TABLE III)

The cancers of the ovary are distinguished by the diversity of their cells of origin, and evidence has been presented in the literature to show that certain of the special types, such as the granulosa cell tumors and dysgerminomas, have a relatively favorable prognosis. For this reason some writers on this subject have considered it wise to exclude these special tumors from series of cases of ovarian cancer on which 5 year end-results are reported. To make this exclusion seems to us to render the record incomplete, for although the special types are probably in general less malignant

TABLE I.—CURE RATES REPORTED FOR CANCER OF THE OVARY

	Total cases	Per cent cure
Schaefer	74	16.2
Stuebler and Brandess	122	24.5
Schleyer	126	9.5
Wintz	87	17.2
Norris and Murphy	93	53.8
Taylor	84	8.3
Schroeder	56	32.1
Heyman	134	32.1
Lynch	62	35.5
Meigs	147	16.0
Pemberton	114	32.0
Walter, Bachman, and Harris	63 (No x-ray) 61 (x-ray)	6.3 29.0

than the adenocarcinomas, they nevertheless do frequently metastasize and cause the patient's death. These tumors should, therefore, be included in any series of cases of cancer of the ovary although tables should be so constructed that the part they play in the final figure for the whole series is apparent.

Adenocarcinomas of the ovary. In the largest group, the papillary serous and pseudomucinous adenocarcinomas, 88 in number, there was a 5 year cure rate of 15.9 per cent. The cure rate among the 25 pseudomucinous tumors was 5 or 20 per cent, among the 63 serous adenocarcinomas, 9 or 14.3 per cent.

Granulosa cell tumors. Of the 16 cases of granulosa cell tumors, 11.6 per cent of the series, there were 5 definite 5 year cures and 7 cases in which the patient died or in which metastasis was present when the patient was last observed. The exclusion of the granulosa cell tumors from the entire series would lower the 5 year cure rate to 13.9 per cent, an insignificant change.

TABLE II.—RESULTS IN RELATION TO EXTENT OF DISEASE

	Total cases	Per cent frequency	Per cent cured
Complete surgical removal	44	31.9	45.5
Partial removal	50	36.2	4.0
Exploration only	29	21.0	0.0
Recurrent cancer	15	10.9	0.0
Total	138	100.0	15.2

Other special tumors. The dysgerminoma is represented in this series by 2 patients, both of whom died of their disease shortly after treatment. There were 2 patients with squamous cancer developing in a dermoid cyst, both of whom also died within a few months of their operation. Four cases classified as mesonephroma (Schiller) resulted in 1 cure and 3 deaths from recurrence.

Metastatic tumors. There were 4 ovarian carcinomas with endometrial cancer in which there was a doubt as to the primary site of the tumor. In this group there was one 5 year cure. In another patient classified with the granulosa cell tumors, there was an independent primary cancer of the endometrium.

In 12 cases originally classed as cancer of the ovary, histological review suggested that the tumor might have originated in the stomach or large intestine. All of these patients

TABLE III.—FREQUENCY AND RESULTS IN INDIVIDUAL TYPES

	Cases	Frequency	Cures	Per cent cured
Papillary serous adenocarcinoma	63	45.6	9	14.3
Pseudomucinous adenocarcinoma	25	18.1	5	20.0
Granulosa cell tumor	16	11.6	5	31.3
Dysgerminoma	2		0	
"Mesonephroma"	4		1	
Cancer in dermoid cyst	2		0	
Associated endometrial cancer	4		1	
Possible gastrointestinal primary	12		0	
Unclassified	10		1	
Total	138			15.2

TABLE IV.—RESULTS IN RELATION TO HISTOLOGICAL GRADE IN ADENOCARCINOMAS

	Total cases	Cures	Per cent cured
Papillary serous adenocarcinoma. Grades 2 and 3.	45	2	4.4
Pseudomucinous adenocarcinoma. Grades 2 and 3.	7	0	0
Papillary serous adenocarcinoma. Grade 1.	18	7	38.8
Pseudomucinous adenocarcinoma. Grade 1.	18	5	27.7
Total	88	14	15.9

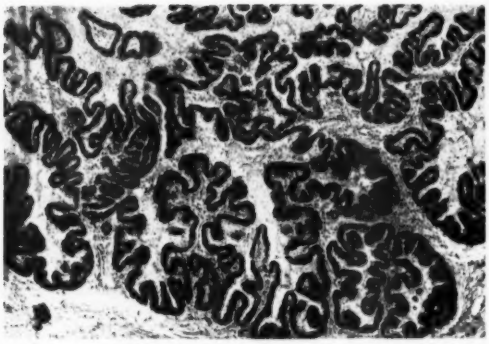


Fig. 1. Papillary serous cystadenoma. Clinically diagnosed as malignant. Ten year cure (B-3867).

Fig. 2. Papillary serous cystadenocarcinoma. Originally diagnosed as benign. Recurrence in 2 years (SC7852).

are dead. The exclusion of these 12 cases would raise the original 5 year cure rate to 17.4 per cent.

Unclassified cases. The histological material was either lacking or unsatisfactory in 10 cases among which there was 1 cure.

It is noteworthy that the exclusion of any of these rather small groups has very little effect on the 5 year cure rate of 15.2 per cent that has been noted for the series as a whole.

HISTOLOGICAL DEGREE OF MALIGNANCY (TABLE IV)

Although it has been repeatedly stated that "grading" has no bearing on the results of treatment in ovarian cancer, most reports indicate that there is a relatively favorable outlook for the more differentiated papillary adenocarcinomas of the ovary (Pemberton, Lynch, Meigs, 6). Other writers, who speak of malignant degeneration in papillary cystadenomas are apparently referring to the same group (Stuebler and Brandess). Still other writers use the term papillary cystadenoma for tumors that have, from the clinical standpoint, a malignant course (Moench). It seems best to us to designate these differentiated types, which are capable at times of recurring and killing the patient, as grade 1 adenocarcinoma of the ovary.

If the recognition and segregation of this type may be termed "grading," then the grade of malignancy in ovarian cancer is of enormous prognostic significance. The classification of 88 cases of ovarian adenocarcinoma, Table IV, indicates only 2 cures, among 52 undifferentiated types whereas among 36 so called grade 1 cases there were 12 cures.

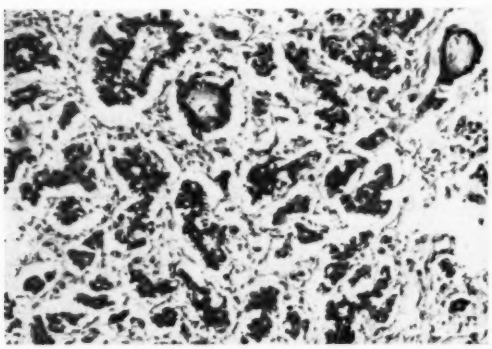


Fig. 3. Infiltrating carcinoma in recurrence from tumor of Figure 2 (SD1949).

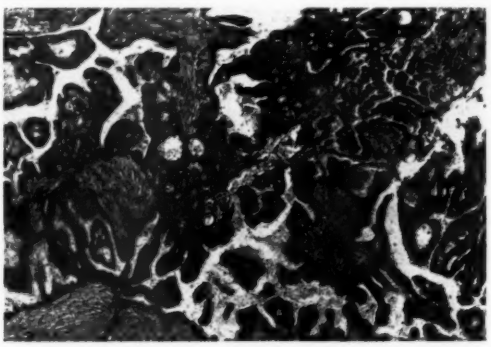


Fig. 4. Papillary serous cystadenocarcinoma. Originally diagnosed as benign. Died after 10 years (SA9775).

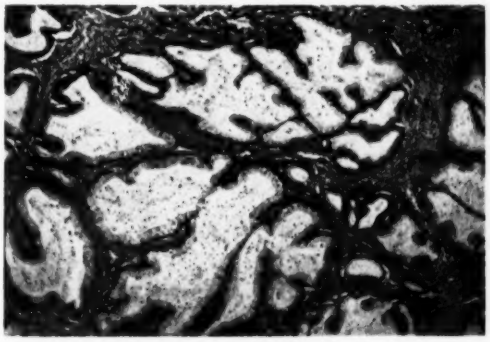


Fig. 5. Pseudomucinous cystadenoma. Originally diagnosed as malignant. Five year cure (SD2724).

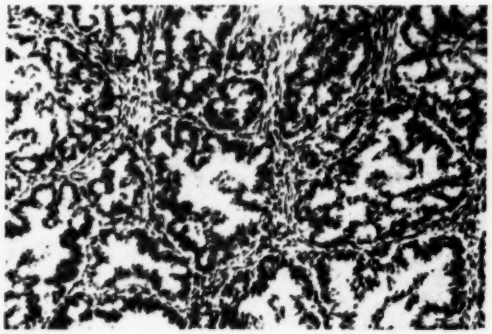


Fig. 6. Pseudomucinous cystadenocarcinoma. Malignancy doubtful. Five year cure (SC9376).

In a series of cystadenomas and adenocarcinomas of the ovary, the morphological transition from the benign to the malignant takes place almost imperceptibly. No pathologist has had the experience to place the line of division exactly. The uncertainty of histological diagnosis in this group of tumors is exemplified by 6 cases.

The following papillary serous tumors are only a part of those about which there was disagreement.

C. F. (No. 2,649, Fig. 1). An unmarried woman of 35 years was operated upon at the Roosevelt Hospital on July 24, 1913. Bilateral cysts of the ovary with multiple intestinal implants were discovered and, although a complete hysterectomy with removal of both adnexa was performed, neoplastic tissue remained in the abdomen. In spite of these findings the patient was quite well 13½ years after her operation. A pathological diagnosis (B-3,867) of papillary cystadenoma was made, and this diagnosis was confirmed by the patient's course.

H. L. (No. 20,489, Figs. 2 and 3). A married woman of 35 years had a right oophorectomy on January 12, 1933, for a small cyst, discovered after operation to be filled with papillary material. On the basis of slides (SD7,852) a diagnosis of "papillary cystfibroadenoma (benign)" was made (Fig. 2). Two years later she was operated upon again and found to have a solid tumor in the right side of the pelvis and metastatic nodules in the abdominal wall and omentum. The diagnosis (SD1,949) was now changed to papillary cystadenocarcinoma (Fig. 3).

H. W. (No. 13,388, Fig. 4). A married woman of 34 years was admitted to the hospital June 19, 1920. At operation an apparently inoperable condition was found and a diagnosis was made of papillary cystadenocarcinoma. The disease did not progress, however, and the uterus and adnexa were successfully removed 18 months later. A histological diagnosis was then made of papillary cystadenoma (SA9,775). She remained well for 3 years after which ascites appeared. Seven years after the beginning of her

Fig. 7. Pseudomucinous cystadenocarcinoma. Originally diagnosed as benign. Died in 13 months (C3181).

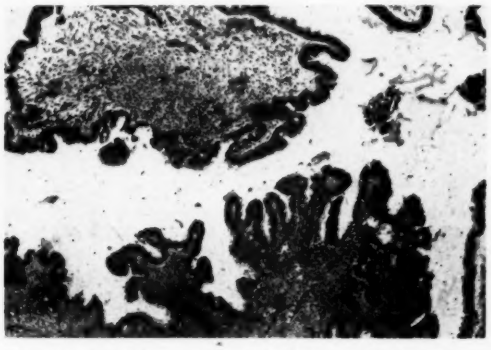


Fig. 8. Papillary serous cystadenoma. Benign type. Ten year cure (SB6723).

Fig. 9. Papillary serous cystadenofibroma. Benign type (SE2616).

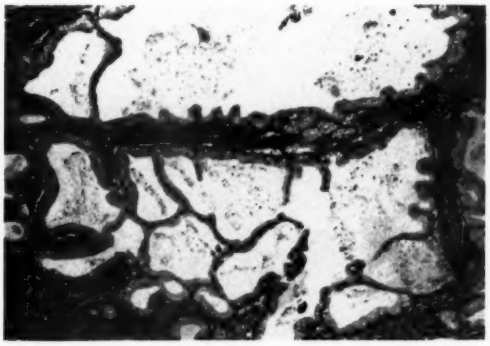


Fig. 10. Pseudomucinous cystadenoma. Benign type (SD_{5534}).

disease an exploratory operation was performed again and in spite of an identical histological structure, the diagnosis was changed back to papillary cystadenocarcinoma. Ten years after the onset of her disease she died.

The pseudomucinous tumors offer similar problems, as can be seen from the following 3 cases.

M. R. (No. C-354,632, Fig. 5). A single woman of 25 years was operated upon on December 16, 1935. A large cystic tumor was found and a right salpingo-oophorectomy was performed. An original diagnosis of carcinoma (S.D.2,724) was made, but this opinion was reversed after outside consultation and the case is now carried in our records as benign. She is free of recurrence after 5 years.

C. C. (No. 21,154, Fig. 6). A married woman of 32 years was operated upon in the fourth month of her pregnancy and a right salpingo-oophorectomy was undertaken. The patient was delivered of a normal child at term and has since remained well. Slides (S.C.9,376) were submitted to four pathologists, who examined them independently. Two regarded the condition as benign and two as malignant. On account of the recognized authority of one pathologist who called this cancer, the case has been carried in our carcinoma series although it is our belief that almost all tumors of this type will be cured.

M. P. (No. 5,637, Fig. 7). A married woman of 60 years was operated upon on November 1, 1915, and a large multilocular cyst of the right ovary was found. The operation consisted in a complete hysterectomy and bilateral salpingo-oophorectomy. No metastasis was present and a diagnosis of papillary cystadenoma was made (C3,181). Nevertheless, the tumor rapidly recurred, causing the patient's death in 13 months. The diagnosis was accordingly changed to adenocarcinoma.

There are then 2 possible changes in our histological classification of cases which would fundamentally affect our own reported cure rates. (a) Certain of the cases classed as papillary adenocarcinoma might have been benign. Actually 12 of the 14 cured cases of adenocarcinoma were regarded as well differentiated and classed as grade 1. (b) On the other hand, some of the 60 papillary cystadenomas were perhaps malignant. There are no known recurrences in this group. Nevertheless, 4 were noted to have had peritoneal implants at the time of their operation and 6 were labelled carcinoma by the first pathologist. In all, at least 26 of the 60 papillary cystadenomas were somewhat doubtful (Table V).

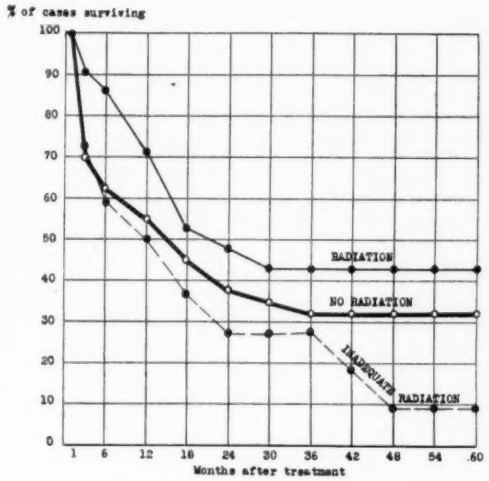
It is interesting to note what an effect changes in the classification of these two categories, those here regarded as grade 1 adenocarcinomas and as doubtfully benign or actively proliferating papillary cystadenomas, would have on the reportable cure rates of the Roosevelt Hospital cases. The exclusion of 12 cured grade 1 cases would have reduced our 5 year rate in the cystadenocarcinoma group

TABLE V.—HISTOLOGY OF PAPILLARY CYSTADENOMAS OF OVARY, 1910–1935

	No. cases
Serous cysts of borderline histology (Fig. 1)	8
Serous cysts with active epithelial proliferation (Fig. 8)	14
Serous cysts with papillary fibroadenomas (Fig. 9)	18
Pseudomucinous cysts of borderline histology (Fig. 5)	4
Benign pseudomucinous cysts (Fig. 10)	4
Inadequate tissue for classification	12
Total	60

to 2.6 per cent; in the entire series of ovarian cancer to 7.9 per cent. On the other hand, if the 26 "borderline" cystadenomas had been added to the cures, the 5 year cure rate of the adenocarcinomas would have been 35 per cent; the cure rate for the entire series, 29.2 per cent. A range of 8 to 35 per cent of 5 year cures in ovarian "cancer" is about what may be found in the literature.

Difference of opinion as to what histological features justify the classification of some of these borderline tumors as benign or malignant, is probably the most important variable governing the reported figures on cures of ovarian cancer. A slight change in conception of the morphological criteria of malignancy in the cystic tumors of the ovary appears to us largely to explain the change in our own figures from the 8.3 cure rate of our 1934 report to the 15.2 per cent noted in the present article.



Graph 1. Effect of x-ray therapy on survival in cases of ovarian cancer.

RADIATION THERAPY

Postoperative x-ray treatment of ovarian cancer was begun at the Roosevelt Hospital in 1928. For the first 3 years the therapy consisted as a rule, in a single high voltage treatment given to each of four fields, but insufficient in amount to produce a skin erythema. From 1931 to 1933 the commonest plan of therapy was based upon four pelvic fields, each receiving 670 r in one dose, the factors being 200 kilovolts; 50 centimeters target-skin distance; 1 millimeter aluminum and 0.5 millimeter of copper filtration; 5 milliamperes of current; for 70 minutes; with fields of 20 by 20 centimeters. From 1933 to the present various plans to give divided dosage have been employed, the commonest being the use of four fields, each receiving five exposures of 300 to 360 r at each treatment. The factors employed for delivery of these treatments were usually 200 kilovolts; 50 centimeters distance; 2 millimeters of aluminum and 0.75 millimeter of copper filtration; 25 milliamperes of current; for 9 minutes with fields of 15 by 15 centimeters. In the tabulation of these cases, those which received 650 r or more per port in a single treatment or a series of small treatments totaling 1500 r or more have been classed as receiving "adequate" radiation and are to be distinguished from those receiving incomplete x-ray courses or small doses of radium in the uterus or vaginal vault.

Among the 82 patients receiving no radiation there were 5 year cures in 12, 14.8 per cent; among the 26 patients receiving "adequate" radiation therapy, there were 5 year cures in 9, 34.6 per cent; and among the 30 patients receiving incomplete radiation there was 5 year cure in only 1, 3.3 per cent. It is noteworthy that all but 2 of the radiation cures are in the relatively differentiated type in which cure frequently results simply from surgery. In 2 cases alone, those in which some carcinoma remained after the conclusion of the operation, x-ray appears to have been the essential factor in producing a cure.

A better method perhaps of studying the effects of x-ray is in the construction of a curve for survival rate (Graph 1). The curve is based on 82 cases, in which patients survived their operation by at least 1 month and in which the exact month of patient's death because of cancer is known. The curve of survival for the patients receiving "adequate" x-ray is consistently higher than the basic curve for the nonradiated cases but is of essentially the same shape. It should be

noted further that, had the deaths within the first 3 months been eliminated, the two curves would have been almost exactly superimposed. The very low survival curve of the cases receiving "inadequate" radiation is probably an example of the range of variation which may be expected in building curves on small samples of cases, but might be due to the fact that it includes a number of patients who were too sick to complete their treatments. It does not appear to us that radiation, as given at the Roosevelt Hospital, has materially affected the average duration of life in cases of ovarian cancer.

Strikingly beneficial effects from x-ray therapy in ovarian cancer have been reported from many sources (Harris and Payne, Heyman, Montgomery and Farrell, Schinz and Zuppinger, Schroeder, Wintz, and Walter, Bachman, and Harris). Yet the best cure rates reported after postoperative x-ray therapy still lie within the limits of the best figures reported for cases not treated by radiation. Furthermore few, if any, reports based on contrasted series treated in the same institution have eliminated the possibility of the favorable selection of patients assigned to radiation. It does seem probable to us that in an occasional case, as 2 cited in this series, the x-ray is the essential factor in producing a 5 year cure, but it appears unlikely that postoperative x-ray can be expected to transform a cure rate of 6.3 per cent to 29.0 per cent, as indicated in the recent paper of Walter, Bachman, and Harris.

SUMMARY AND CONCLUSIONS

1. The reporting of statistics on ovarian carcinoma, on account of the heterogenous character of the disease, requires the listing of special types with their individual end-results as well as figures for the whole. The special types, such as granulosa cell tumors and dysgerminomas, should be placed in special categories. The adenocarcinomas should be graded and at least those capable of different interpretation by different pathologists considered as a group. In this respect it is necessary to include a note on the papillary cystadenomas treated in the hospital during the same period, since if this group is very small it is probable that some have been erroneously classed with the cancer cases. Tumors possibly primary outside of the ovary should not be disregarded, simply because the primary ovarian character cannot be absolutely established.

2. In the present series of 138 cases of ovarian cancer the absolute 5 year cure rate is reported as 15.2 per cent. The factor which most affected prognosis was the gross stage of the disease at the time of operation. Of next importance was the histological grade of the tumor, at least in the sense that the differentiated tumors of perhaps doubtful malignancy had a very much better prognosis than the others.

3. Postoperative x-ray therapy was apparently responsible for the 5 year cure of 2 cases, in which recurrence was otherwise certain, but the effect of x-ray on the percentage of 5 year cures and on survival curves was less than has been frequently claimed.

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FRACTURES OF THE FOREARM

Some Technical Procedures

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REDUCTION, retention, and restoration of function are the basic principles of fracture therapy. The techniques developed from these broad themes are legion. In their little details lies ultimate success or failure. Perhaps in no other branch of surgery do trifles loom as great. Our methods of dealing with two common forearm fractures do not infringe on basic principles: they have helped with trifles.

In the ubiquitous Colles' fracture, the great postreduction problem is circulatory obstruction. Originally I splinted these fractures with circular plaster, attempting to make the cast thin enough that, when split on the ulnar side, it would yield to the swelling wrist. Good in theory, the figure of eight windings around wrist and hand made an unavoidably rigid plaster. Forcing its cut edges apart was difficult and sometimes resulted in a loss of the reduction. The simple dorsal or ventral plaster mold did not give the desired stability. Hence, the spiral mold.

The mold (Figs. 1, 2, 3) is made of one to two 3 inch by 3 yard bandages. The crinoline-impregnated type is most satisfactory, giving greater strength per ounce. The mold is rolled dry; the distal end is cut obliquely to make a narrow strip across the palm. It is dipped in water, and applied without padding—this is essential. Beginning on the palm, embracing the hypothenar eminence, its distal edge follows the proximal crease of the palm till it passes between thumb and index finger. The angulated edge (made by cutting the end of the mold) is radial, and ends just distal to the radial styloid, so that the full width of the plaster covers the site of the fracture. The mold is continued around the arm to end just distal to the medial epicondyle of the humerus.

The mold is held in place by a wet gauze bandage, the palmar strip being shaped well to fit the palmar arch.

In most cases swelling of the hand will be so slight as to demand no interference. The patient may be sent home without fear of an ischemia developing over night. If swelling does become troublesome it must be relieved. The gauze bandage is cut along the lateral border of the hypothenar eminence, the plaster and injured wrist are supported firmly on their dorsum, the palmar strip of plaster is levered free from its hypothenar end, and then restrapped less tightly. The fracture area has not been disturbed.

After 10 to 14 days the spiral mold is replaced by a simple dorsal mold with the hand in dorsiflexion.

It may be observed in Figures 2 and 3 that the hand is not in the position of flexion too often shown as the correct one for holding a Colles' fracture in reduction. Originally described by Cotton, the technique of reduction has grown to a beautiful example of surgical mechanics. The first movement is pronation. Through the leverage of the hand and carpal ligaments this forces the distal, radial fragment downward, ventrally. The second movement of ulnar deviation, by traction on the radial-carpal ligaments, opens the

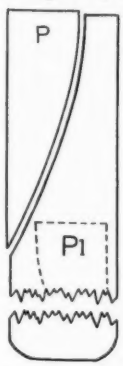

Fig. 1. Fragment *P* serves to reinforce the mold over the wrist joint at P_1.

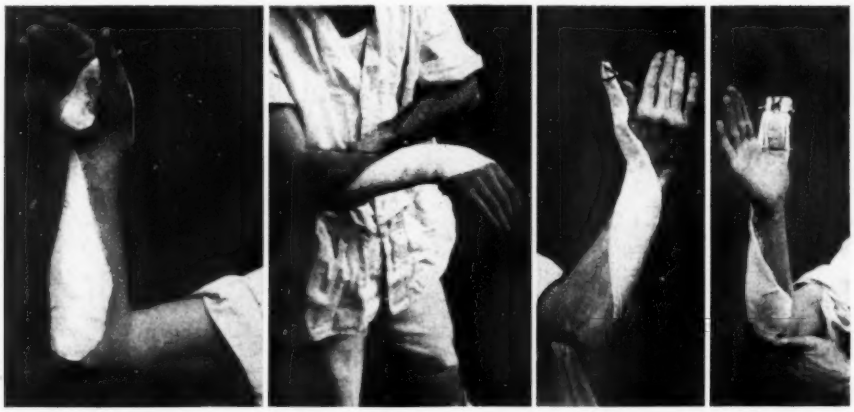

Fig. 2. Fig. 3. Fig. 4. Fig. 5.

Figs. 2, 3, 4, 5 are posed by internes, as the mold when applied to a fractured arm must be bandaged on. Obviously, the Kirschner wire in Figure 5 does not pierce the phalanx.

space into which it descends; it also corrects the lateral displacement. The third movement, flexion, in this position is limited to about 25 degrees. It simply locks the distal fragment in place and helps to correct the dorsal tilt of its articulating surface.

The spiral mold was devised originally to overcome a problem met in treating fractures of the phalanges and metacarpals, particularly Bennett's fracture at the base of the first metacarpal. Abduction of the thumb rarely gives a satisfactory reduction without traction. In using a wire, projecting from a plaster arm cuff, to take the traction through an elastic band to the Kirschner wire in the proximal phalanx, we found that the cuff (pushed tight by countertraction) often caused circulatory obstruction in the arm. The spiral mold (Figs. 4 and 5), bandaged with wet gauze, grips without squeezing. The extension along the dorsum of the thumb splints as well as giving a base for traction.

Fig. 6. The patient holds the arm, unsupported, in abduction. The apparatus is not heavy.

Absence of padding under these molds is essential. It permits the myriad hairs of arm and hand to serve as anchors. I have given up, in all plaster work, the use of sheet wadding. When padding is necessary, over bony points, and on plaster margins, saddler's felt or sponge rubber serves best. If no padding be needed, none is used. A smoothly molded plaster is kinder to the skin than the undulating vagaries of sheet wadding.

The apparatus for reducing fractures of the radius and ulna is presented with distinct reservations. These fractures of both bones may be divided, therapeutically, into two broad groups: those which respond to closed manipulation and those which do not. It is desirable that the first group be as large as possible. The use of good local, or deep general anesthesia, manipulation under the fluoroscope, prolonged traction to tire spastic forearm muscles—these will increase its numbers. A certain proportion of cases must fall into the operative class.

In between are those that respond to skeletal traction. Let us add to their number a group of cases we have all met—the old, ill treated, ununited fractures of radius and ulna,

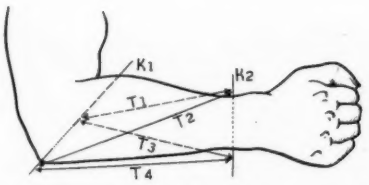

Fig. 7. *K1*, Kirschner wire through the proximal end of the ulna, at right angles to *K2*, through the distal ends of radius and ulna. *T1*, *T2*, *T3*, *T4*, turnbuckles.

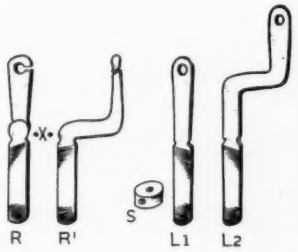

Fig. 8. *R*, *R*1—2½ inch right hand threaded end for turnbuckles. 4½ inch and 6½ inch pieces are identical, but lengthened at *X*. *L1*, Left hand threaded ends for turnbuckles *T3* and *T4*. *L2*, Left hand threaded ends for turnbuckles *T1* and *T2*. *S*, Stop, with setscrew, for Kirschner wire.

in which powerful flexor muscles have contracted and overcome the extensors to produce marked angulation at the site of the fracture—an angulation that must be corrected before good operative work can be done. It was in such cases that our turnbuckle apparatus (Fig. 6) was first used. We have since used it in selected, fresh fractures, with good results.

Kirschner wires are used according to the common technique. One is drilled through the proximal end of the ulna; one through the distal ends of radius and ulna. These wires are at right angles to one another when the hand is midway between pronation and supination. (This is not only the position of optimum function, it is the position of best muscular balance and the one in which radius and ulna are most nearly parallel.)

On the Kirschner wires are mounted four turnbuckles (Fig. 7, *T1*, *T2*, *T3*, *T4*). Thus they form four triangles of force, two with their bases on the radius-ulna wire, two with their bases on the olecranon wire. Manipulation of the fractured bones is possible in all planes. They are held stable in any position without further splinting.

The apparatus and its application in detail: Four 3½ inch turnbuckles are used. These have a range between contraction and expansion, of 2½ inches. Three sets of right hand threaded ends are made for each turnbuckle—2½ inch, 4½ inch, 6½ inch (Fig. 8), giving for the set a continuous range from 5 to 11½ inches, to fit children and adults. Channels are cut to the Kirschner wire openings in the right hand threaded ends to permit changing sizes, without opening the stirrup. This is rarely necessary. The right hand threaded ends are offset three-quarters of an inch to allow for the curve of the arm. On two of the turnbuckles, for *T1* and *T2*, Figure 7, the left hand threaded ends are also offset ¾ inch, and are ¾ inch longer, to compensate for the added length of their diagonal direction. Four stops with set screws are provided to prevent the Kirschner wires from slipping in the bone if unequal stress be put on them.

The Kirschner wires are drilled through distal radius and ulna, and through the proximal ulna. Sterile, saddler's felt "washers" are mounted on each side of each wire, against the skin. The stops are set on the wires. The turnbuckles follow; the wires are drawn taut in stirrups. The proximal stirrup can be slung to the posterior surface of the upper arm by adhesive. The distal rests best on the dorsum of the forearm. The turnbuckles are now adjusted to reduce the fracture. Obviously, to correct bony angulation, lengthening of one turnbuckle will necessitate simultaneous lengthening of one other, and shortening of the remaining two. Thus, if there be an ulnar convexity, lengthening of *T1* and *T2* must be accompanied by shortening of *T3* and *T4*. Uniform traction is applied by making equal stress on all four. As with any form of screw traction, the danger of over extension must be guarded against. Fluoroscopic control of manipulations is desirable.

With a satisfactory reduction confirmed by x-ray examination, arm and apparatus may be supported in an ordinary sling. When the patient is in bed the arm should be supported on the chest by pads; otherwise there is danger of pressure on the medial stop on the

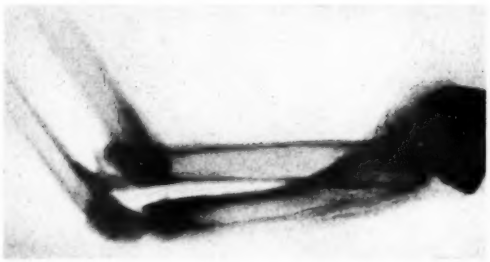

Fig. 9. Case 2, December 18, 1940.

olecranon wire, pushing it against the skin. The patient is allowed active movements of wrist and elbow (the latter is limited to 25 degrees). These movements are painless and seem to cause no abnormal mobility at the fracture line. Despite this apparently complete immobilization, I have not depended on the apparatus alone for splinting beyond the first two weeks. Perhaps this is an unnecessary precaution. I do not yet know. At the end of that time, turnbuckles are removed and plaster applied from the insertion of the deltoid to the proximal crease of the palm, incorporating the wires.

If desired, plaster may be applied immediately following reduction. In this event it is better to use the large Kirschner stirrups, to facilitate the application of the plaster beneath the turnbuckles.

Three cases in which the use of the turnbuckles was particularly indicated:

CASE 1 (Victoria General Hospital, No. 26294, Fig. 6). The patient, aged 43 years, was admitted with a fracture of radius and ulna in the middle third. Both fractures were oblique. The radius showed very slight displacement; the ulnar fragments were overriding with angulation. The elbow joint was the seat of an osteoarthritis. To lessen the immobilization time of the elbow, reduction was made with the turnbuckle apparatus and movements of elbow and wrist were permitted, for 2 weeks. X-ray examination at this time showed early callus formation. A plaster was then applied from deltoid insertion to the proximal crease of the palm, incorporating the wires. The turnbuckle apparatus was removed.

CASE 2 (Victoria General Hospital, No. 26463). The patient, male, aged 26 years, was admitted with a fracture of the radius and ulna, at the upper and middle third, of a year's standing; union was fibrous. Flexor contraction had resulted in 70 degrees' angulation at the site of the fracture (Fig. 9). Manual traction and massage were given without result. December 19, 1940, the turnbuckle apparatus was applied. Adjustments were made to stretch the contracted muscles, the turnbuckles being given a few turns every 2 or 3 days. February 5, 1941, the angulation was almost completely corrected (Fig. 10). The arm was prepared for operation to freshen the bone ends and fix them internally. After operation the apparatus was reapplied to prevent recurrence of contraction.

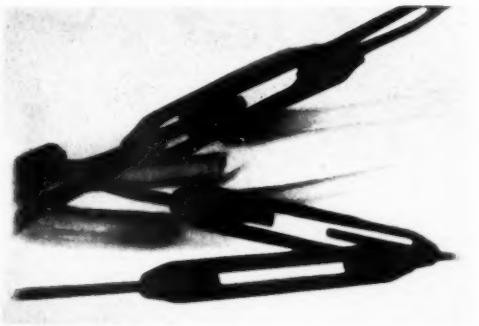

Fig. 10. Case 2, February 5, 1941.

CASE 3 (Halifax Infirmary, No. 1250-39). The patient, male, aged 52 years, had an ununited fracture of the radius and ulna at their middle thirds. There was 15 degrees of ulnar convexity at the site. Operation was performed. The bones appeared healthy; the ends were freshened, perforated with multiple drill holes, and wired. The bones were held straight with little effort. Incisions were closed and a plaster cast was applied over light dressings. X-ray films taken at the end of 3 weeks showed good callus formation, but a return of the angulation, although the cast had not been disturbed. The cast was removed. Kirschner wires and the turnbuckle apparatus were applied, the angulation was corrected and so held till firm bony union.

SUMMARY

Presented as useful adjuncts to fracture therapy are:

1. A spiral plaster mold for fractures of the lower end of the radius, the metacarpals and phalanges, which grips and immobilizes the part without causing circulatory interference.

2. An apparatus for reduction of fractures of radius and ulna which consists of four special turnbuckles mounted on Kirschner wires through distal radius and ulna, and through proximal ulna, so as to give control of the fragments in all planes.

THORACOSCOPY AND PNEUMOLYSIS

Observations on One Hundred Consecutive Cases

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New York, New York

RIVERSIDE HOSPITAL is one of the New York city municipal institutions for the tuberculous in which far advanced cases constituted about 72 per cent of the admissions during the past 5 years. During this same period 69 per cent of the patients were colored. In most of the cases pneumothorax therapy had been initiated elsewhere. In many instances thoracoscopy and pneumolysis were carried out as a last resort in patients with bilateral disease in the hope that some clinical improvement might be produced by cutting adhesions to help in the collapse of a cavity and the conversion of sputum. It is apparent, therefore, that we have had the more unfavorable type of material for these procedures. No patient was operated upon except after consultation with the medical service, directed by Dr. Max Taschman, and such specialty services as were indicated. We shall report our observations and follow-up notes on our first 100 consecutive patients who had thoracoscopy or pneumolysis.

TECHNIQUE

The instrument. About 95 per cent of the pneumolyses were performed with the Moore apparatus, by the use of thoracoscopy through one opening into the pneumothorax cavity and by division of the adhesions through another opening with an electrode which carried coagulating and cutting currents. The Coryllos instrument with its actual cautery was used for the remainder of the cases. All instruments are tested carefully before operation to make sure that the light bulb, cable connections, and current are in working order. On a number of occasions, unnecessary bleeding was produced by a defective current as a result of improper electrical connections. A blurred field of vision may result from a moist ocular, from insufficient current, from a cold light bulb or observation lens or their moistening by blood or intrathoracic fluid. Appropriate measures correct all of these conditions.

The position of the patient. In most instances the patient was placed on his back with a pillow beneath the shoulders. The head was hyperextended and turned to the side opposite the operative field. The hand on the side of the operative field was placed beneath the head. There was no hesitation in sitting the patient up or turning the trunk if such positions produced a better view of the adhesions and easier intrathoracic manipulation.

Anesthesia. Local novocain anesthesia was used exclusively with especial care to infiltrate the parietal pleura.

Thoracoscopy openings. In over 90 per cent of the cases, openings into the second interspace in the midclavicular line and the third interspace in the midaxillary line were found adequate for thoracoscopy and pneumolysis. When indicated, openings were made in any other part of the chest wall. Stab wounds through the intercostal space permitted the snug introduction of the trocar and cannula. In this way postoperative emphysema of the chest wall and adjacent tissues was minimized or prevented, especially if the edges of the stab wound were tightly approximated by deep suture.

Division of adhesions. Pneumolysis requires patience and meticulous care and any attempt at hurry may produce a disastrous complication or incomplete therapy. The ideal time for cutting adhesions seemed to be as early as possible, when the mediastinum was already stabilized by the pneumothorax and when

From the Surgical Service of Dr. Louis Carp, Riverside Hospital.
Read before the Section on Surgery, New York Academy of Medicine, November 7, 1941.

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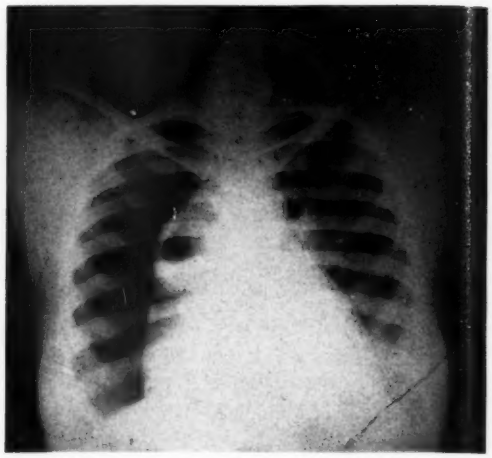

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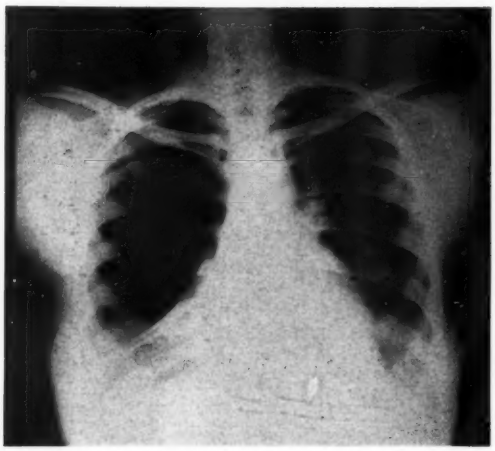

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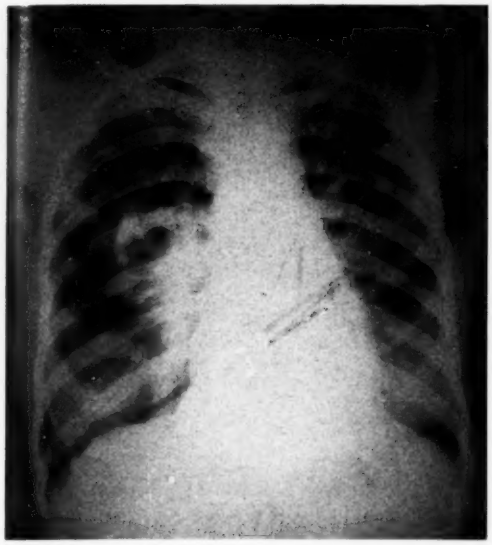
Fig. 1. Successful collapse of cavity following pneumolysis. Colored female, aged 17 years, duration of symptoms 6 months; duration of pneumothorax, 3 months. a, Unilateral pulmonary tuberculosis with cavity 3 centimeters in diameter in right upper lobe. Note what were interpreted as two string adhesions running from the upper lobe toward the first rib. Thoracoscopy showed a thick columnar adhesion which fanned out at the apex of the thoracic cage. Pneumolysis. b, Roentgenogram 27 days after operation to show beginning collapse of the cavity aided by continued pneumothorax refills. Note spread of disease in the hilar region of the contralateral lung. This was temporary. c, Roentgenogram 9 months after operation to show complete collapse of the cavity. The sputum was converted 4 months after operation. A 26 months' follow-up shows involvement of the contralateral lung and partial expansion of the right upper lobe which contains a cavity. Sputum is positive.

this was adequate for intrathoracic visualization and instrumental manipulation. Wherever possible, we attempted to cut adhesions near the chest wall. At this point there is less danger of injury to lung and adjacent anatomical structures and usually there is less bleeding. At times enucleation of the adhesion from the chest wall was advisable. At other times partial pneumolysis was performed under the following conditions: technical difficulty, too lengthy an operation, or a desire to stretch an incompletely divided adhesion by increased intrathoracic pressure so that its complete division at a later date would be easier. Pneumolysis in stages was performed in 9 of our cases. In 5 of these there were 2 procedures and in 4 there were 3.

Postoperative care. Patients were kept in bed and given fluids for 24 hours with codeine for sedation and to diminish the cough reflex. Pneumothorax refills were continued within the first 24 hours after operation.

THE ADHESIONS

Location. We tried to correlate the locations of adhesions by roentgenogram and



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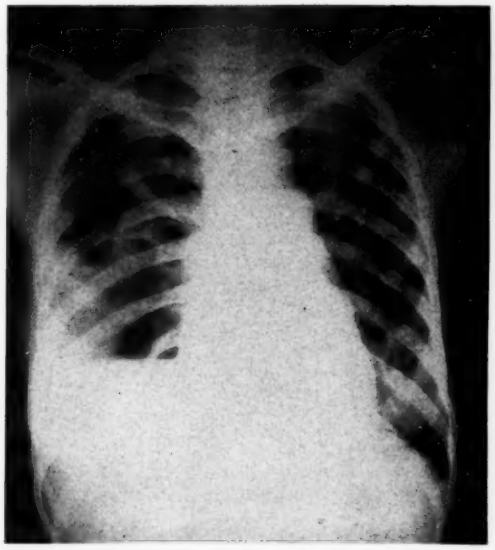

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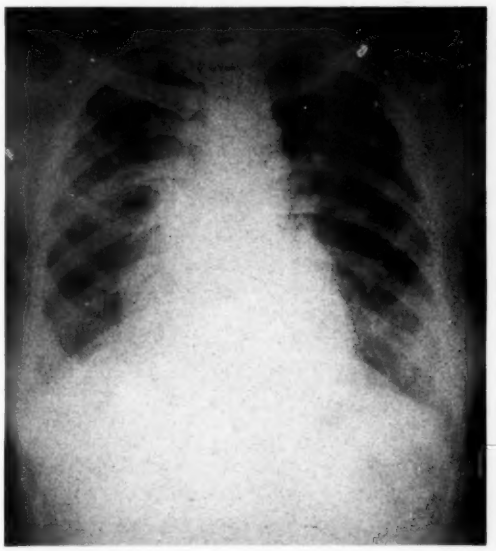

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Fig. 2. Partial pneumolysis with subsequent bilateral pulmonary fibrosis and conversion of sputum. Colored female, aged 24 years; duration of symptoms, 6 months; duration of pneumothorax 3 months. a, Bilateral pulmonary tuberculosis, with cavity 3 centimeters in diameter in the right upper lobe. Note what was interpreted as massive apical adhesions and string adhesions running toward the second rib. Thoracoscopy showed thirteen string adhesions. Partial pneumolysis. Patient developed a right hydrothorax promptly and contralateral spontaneous pneumothorax 10 days after operation. b, Roentgenogram 3 weeks after operation to show partial collapse of the right upper lobe and fluid in the right pleural cavity. The sputum was converted at this time. c, Roentgenogram 15 months after operation to show re-expansion of the lung and bilateral fibrosis. The patient is symptomatically improved and the result is probably not attributable to the original operative procedure.

thoracoscopy. In about 90 per cent of the cases this correlation showed that the roentgenogram was only partially accurate, but it usually served as a guide for the position of the main adhesions. Usually, thoracoscopy showed more adhesions than indicated by roentgenogram and very often the roentgenogram could not predict their direction. As a rule, mediastinal adhesions could not be visualized in the chest film.

Character and shape. In the majority of the cases these could not be foretold by roent-

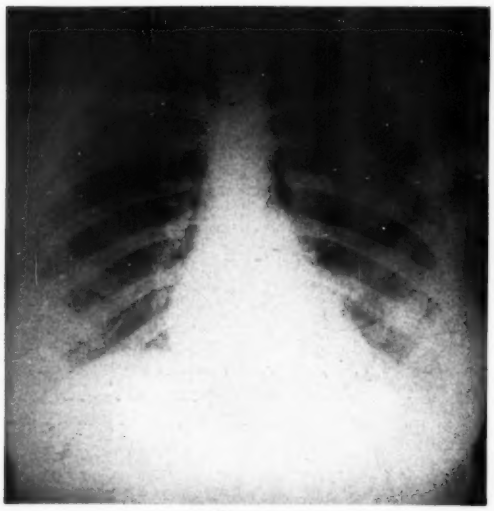

Fig. 3a.

Fig. 3b.

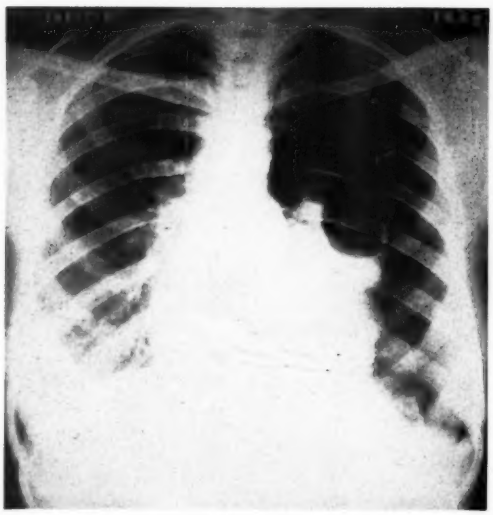

Fig. 3c.

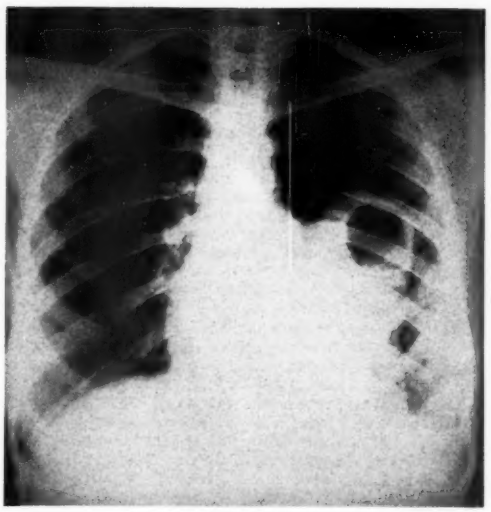

Fig. 3d.

genogram. The interpretation of what appeared to be a string adhesion in the film, very often proved to be a thick spool, plicated, or quadrangular adhesion. In other instances what looked like a divisible adhesion on the roentgenogram proved to be indivisible because of its character, shape, or anatomical position or because of a complete synechia between the lung and chest wall. On the contrary, what looked like an indivisible adhesion on the roentgenogram was often divisible. We have learned, therefore, that it is generally advisable to use thoracoscopy in order to determine the pathological state in the pneumothorax cavity, and to decide at the time of operation whether pneumolysis is feasible. Adhesions, according to shape, conformed to the following descriptions in their order of fre-

Fig. 3. Three stage pneumolysis with collapse of large cavity and conversion of sputum. Colored female, aged 30 years; duration of symptoms, 3 months; duration of pneumothorax, 2 months. a, Unilateral pulmonary tuberculosis with left apical cavity 4 centimeters in diameter and what was interpreted to be a cord adhesion running toward the first rib and massive adhesions between the upper lobe and the mediastinum. Partial pneumolysis, with division of one cord adhesion. b, Roentgenogram 6 days later to show the cavity still suspended by what appeared to be a cord adhesion. Thoracoscopy 2 months after the first operation showed tubercles on the surface of the lung. Pneumolysis of two more adhesions. c, Roentgenogram 1 month later to show what appeared to be a cord adhesion running from the apex of the cavity to the mediastinum and another adhesion running from the lateral border of the cavity to the first interspace. The cavity has dropped and there is a small amount of fluid in the pleural cavity. Pneumolysis of these adhesions 8 days later. This was the third operative procedure. d, Roentgenogram 6 days later and 4 months after the first operation to show complete division of the restraining adhesions with release of the upper lobe and re-expansion of the left lower lobe. e, Roentgenogram 15 months later and 18 months after the first operation to show collapse of the cavity. The sputum was converted 6 months after the last operation.

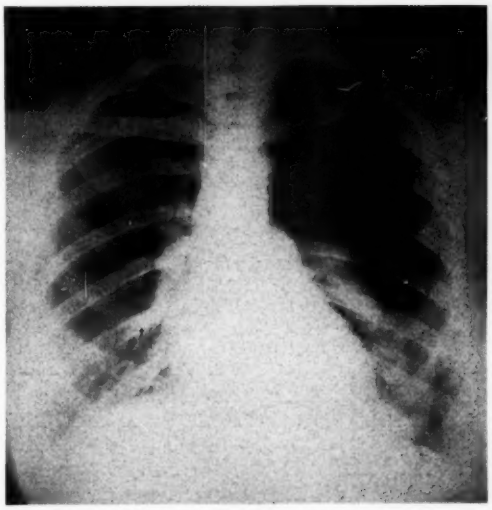

Fig. 3e.

quency (Table I): string, fan, cord, spool, synechia, pyramidal, quadrangular, band.

OBSERVATIONS FROM STATISTICAL ANALYSIS

The following represents some of the more important observations resulting from analysis of our statistical data.

Among 100 consecutive cases that came to operation there were 32 complete pneumolyses, 43 partial pneumolyses and 25 thoracoscopies (Table II). By complete pneumolysis we mean the division of all visible restraining adhesions. By partial pneumolysis we mean an incomplete division of one or more adhesions, or the complete division of a fraction of the total number of adhesions visualized. The average age for the entire series was 29 years; the youngest patient was 14 and the oldest 53 years. Thirty per cent were males and 70 per cent females. Eighty-nine per cent were of the colored race and 11 per cent were white. The average duration of symptoms on admission to the hospital was 11.28 months. At the time of operation, the average duration of the disease was 18 months and the average duration of the pneumothorax was 7½ months. On admission, the sputum was positive for tubercle bacilli in all of the patients. At the time of operation the sputum was positive in 88 per cent of the cases with evidence of cavitation in all. Cavities had an average diameter of 3.5 centimeters. Seventy-six per cent of the patients had bilateral disease and in the remaining 24 per cent it was unilateral (Table III). The average estimated extent of the pneumothorax was about 60 per cent; the smallest 30 per cent, and the largest 90 per cent. Two hundred and ninety-seven adhesions were seen at operation, and 60 per cent of these were divisible. Besides adhesions, thoracoscopy demonstrated the aorta, the subclavian and innominate vessels, the beating heart and the pericardium, the phrenic and vagus nerves, fibrin bodies, purulent and nonpurulent fluid, tubercles and fibrinous exudate on the visceral pleura, and the diaphragm (Table IV).

In the 32 patients who had complete pneumolysis, the sputum was converted and the cavity closed in 62 per cent. In 4 per cent the sputum was converted but the cavity remained open. The cavities collapsed in an average time of 36 days and the sputum was converted in an average time of 60 days. In the 43 cases which had a partial pneumolysis, the sputum was converted and the cavity closed in 30 per cent. The cavities collapsed in an average time of 64 days and the sputum was converted in an average time of 75 days.

TABLE I.—THORACOSCOPIC TYPES OF ADHESIONS

	Complete pneumolysis	Partial pneumolysis	Thoracoscopy only	Grand total	
				No.	Per cent
Fan-shaped	23	49	3	75	25
Cord	18	23	7	48	16
String	16	72	8	96	32
Spool	8	10	2	20	7
Pyramidal	3	9	2	14	5
Columnar	3	0	0	3	1
Quadrangular	2	8	2	12	4
Band	0	4	5	9	3
Synechia	0	7	13	20	7
Total	73	182	42	297	100

TABLE II.—FOLLOW-UP RESULTS

	Complete pneumolysis 32 cases Per cent	Partial pneumolysis 43 cases Per cent	Thoracoscopy only 25 cases Per cent
Sputum converted	67	30.8	36
Cavity closed	62.5	30.2	36
Improved	57	28	28
Sputum positive	33	70	64
Cavity open	37.5	69.8	64
Unimproved	43	72	72
Complications	78	70	64
Died	28.2	26	27

In the 25 cases which had thoracoscopy, the sputum was converted and the cavity closed in 36 per cent. The cavities collapsed in an average time of 110 days and the sputum was converted in an average time of 90 days. The reasons for these last results after thoracoscopy were increased pressures from fluid or pneumothorax, spontaneous rupture of adhesions, phrenemphraxis, and spontaneous fibrosis and recession of the disease. It becomes apparent, therefore, that the length of time for the closure of cavities and conversion of sputum increases in the procedures in the following order; complete pneumolysis, partial pneumolysis, and thoracoscopy. We have also noted that conversion of sputum usually occurs about 1 month after the collapse of the cavity.

Seventy-one per cent of all the cases had complications which were similar in all 3 procedures. At first glance this percentage seems unusually high, but we have included cases with innocuous hydrothorax which constituted almost half of all the complications. These, in their order of frequency, were: hydrothorax (innocuous), spread of infection to the contralateral lung, tuberculous empyema, spontaneous pneumothorax, hemoptysis, hemothorax, and pleurocutaneous fistula.

Tuberculous empyema occurred in 19 per cent of the entire series and mixed infection in 3 per cent. Only 2 of the entire group occurred directly after operation. Seven of

TABLE III.—DISTRIBUTION OF PULMONARY LESIONS

	Complete pneumolysis		Partial pneumolysis		Thoracoscopy only		Grand total	
	right	left	right	left	right	left	No.	Per cent
A. Unilateral disease with cavity no pleural fluid	6	4	0	2	3	6	21	21
B. Unilateral disease with cavity with pleural fluid	0	1	0	0	2	0	3	3
Total							24	24
C. Bilateral disease with cavity no pleural fluid	10	7	15	14	7	5	58	58
D. Bilateral disease with cavity with pleural fluid	2	2	4	8	1	1	18	18
Total							76	76
Total	18	14	19	24	13	12	100	100

TABLE IV.—ADDITIONAL THORACOSCOPIC FINDINGS

	Complete pneumolysis	Partial pneumolysis	Thoracoscopy only	Grand Total	
				No.	Per cent
Adhesions to subclavian vessels	3	2	3	8	8
Fibrin bodies	3	0	0	3	3
Tubercles on visceral pleura	3	4	8	15	15
Fluid in pleural cavity	3	0	5	8	8
Adhesions to aorta	1	0	0	1	1
Lung covered with fibrin and tubercles	1	0	9	10	10
Pericardial adhesions	0	2	0	2	2
Adhesions to innominate vessels	0	1	0	1	1

TABLE V.—POSTOPERATIVE COMPLICATIONS

	Complete pneumolysis		Partial pneumolysis		Thoracoscopy only		Grand total	
	No.	per cent	No.	per cent	No.	per cent	No.	per cent
Total number	25	78	30	70	16	64	71	71
No complications	7	22	13	30	9	36	29	29
Early complications 1–2 months postoperatively								
Hydrothorax	8	24	15	37.5	7	28	30	30
Tuberculous empyema	1	3	1	2.5	0	0	2	2
Spread to contralateral lung	2	6	1	2.5	1	4	4	4
Hemothorax	2	6	0	0	0	0	2	2.
Spontaneous pneumothorax	1	3	0	0	0	0	1	1
Total								37
Late complications—2–31 months postoperatively								
Hydrothorax	4	12	5	12.5	2	8	11	11
Empyema								
Tuberculous	5	15	5	12.5	7	28	17	17
Mixed	2	6	1	2.5	0	0	3	3
Pleurocutaneous fistula	2	6	1	2.5	0	0	3	3
Spread to contralateral lung	4	12	11	27.5	2	8	17	17
Spontaneous pneumothorax	5	15	4	10	0	0	9	9
Hemoptysis	1	3	0	0	2	8	3	3
Tuberculosis of chest wall at site of trocar opening	1	3	0	0	0	0	1	1
Tuberculous laryngitis	2	6	1	2.5	1	4	4	4
Tuberculous enterocolitis	1	3	2	5	1	4	4	4
Total								63
Died	9	28.2	11	26	7	28	27	27

the 22 empyemas followed thoracoscopy (Table V).

There were 7 cases of spontaneous pneumothorax and they predominated after complete pneumolysis. This complication arose early only once after the operative procedure (Tables IV and V). Postoperative emphysema was not troublesome.

The average follow-up time was 10 months in all the cases the longest period being 28 months the shortest 1 month.

The early and late death rate in the entire group was 27 per cent, and it was practically identical in complete or partial pneumolysis and in thoracoscopy. The causes of death in their order of frequency were:

TABLE VI.—CAUSES OF DEATH

	Complete pneumolysis		Partial pneumolysis		Thoracoscopy only		Grand total	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Type of disease								
Unilateral	0		0		0		0	
Bilateral	9	28	11	26	7	28	27	27
Spontaneous pneumothorax tuberculous empyema, bronchopleuro cutaneous fistula	3		0		0		3	
Spread of disease in both lungs	3		9		2		14	
Tuberculous empyema	2(1*)		2		0		4	
Spontaneous pneumothorax	1*		0		0		1	
Hemothorax	0		1*		1		2	
Tuberculous laryngitis	0		1		1		2	
Tuberculous enterocolitis	0		1		1		2	
Hemoptysis from opposite lung	0		0		1		1	
Cardiac failure	0		0		1		1	

*Operative deaths.

Spread of the disease in both lungs, 14; tuberculous empyema, 4; spontaneous pneumothorax, tuberculous empyema, bronchopleurocutaneous fistula, 3; hemothorax, 2; hemoptysis, 1; spontaneous pneumothorax, 1; and cardiac failure, 1. There were 3 deaths which could be attributed to the operative procedure. One patient died during operation from hemorrhage produced by injury to one of the large blood vessels by the electrode.

TABLE VII.—RESULTS OF SPUTUM EXAMINATION

	Complete pneumolysis		Partial pneumolysis		Thoracoscopy only		Grand total	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Converted from positive to negative	14	67	12	30	9	36	35	40
Remained positive	9	33	28	70	16	64	53	60
Total	23		40		25		88	100
Sputum negative before operation	9		3		0		12	
Progress of Cavity								
Cavity closed	20	62.5	13	30.2	9	36	42	42
Cavity remained open	12	37.5	30	69.8	16	64	58	58

VIII.—COMPARISON OF PERIOD OF TIME ELAPSED BETWEEN OPERATIVE PROCEDURE, CLOSURE OF CAVITY AND CONVERSION OF SPUTUM

	Days after complete pneumolysis	Days after partial pneumolysis	Days after thoracoscopy only	Grand average days
Cavity collapsed				
Average period	36	64	110	70
Shortest period	1	2	60	1
Longest period	180	180	150	180
Sputum converted				
Average period	60	75	90	75
Shortest period	7	30	60	7
Longest period	120	60	180	180

This occurred early in our experience. Another death occurred 2 months after operation from hemothorax with empyema which developed 6 days after operation. There was no bleeding at the time of operation. A third patient died from spontaneous pneumothorax 10 days after operation. Of the 27 patients with bilateral disease 24 died from causes not due to operation, in an average time of 9 months (Table VI).

Before operation, 12 patients had a negative sputum despite cavitation with adhesions. It seemed advisable to cut these adhesions. One patient developed a contralateral spread of the disease with a hydropneumothorax. Nine months later the sputum became positive and a tuberculous empyema developed on the side operated upon. Another patient had a persistently negative sputum for 6 months after pneumolysis. This patient died of a spontaneous pneumothorax on the contralateral side.

Tubercles without accompanying exudate could be visualized beneath the visceral pleura in 15 per cent of the cases. Over a follow-up period of from 4 to 28 months, 2 of these patients developed pleural fluid which contained tubercle bacilli. In 1 case the fluid appeared 11 months after partial pneumolysis and in the other patient it appeared 5 weeks after thoracoscopy. Aspiration therapy helped in the disappearance of the fluid in both cases. We believe, therefore, that tubercles on the surface of the lung do not contraindicate pneumolysis, unless they are subject to injury by the electrode.

SUMMARY

1. Our observations are based on complete or partial pneumolysis or thoracoscopy in our first 100 consecutive cases of pulmonary tuberculosis among whom 76 per cent were classified as far advanced and 89 per cent were of the colored race.

2. In most of the patients pneumothorax therapy had been initiated elsewhere, so that the average duration of this therapy was 7½ months before operation. This period is far too long if more successful results are to be obtained. Restraining adhesions should be cut as soon as the pneumothorax has stabilized the mediastinum and when it is adequate for visualization and intrathoracic manipulation of instruments.

3. The roentgenogram of the chest served only as a guide for the approximate location, shape, and potential divisibility of adhesions, but it did not predict these with any degree of accuracy.

4. Thoracoscopy and electrode openings were usually found to be adequate when made in the second intercostal space in the midclavicular line and in the third intercostal space in the midaxillary line.

5. Thoracoscopy is advisable to determine the pathological state in the pneumothorax cavity and also the feasibility of pneumolysis. Thoracoscopic findings are enumerated.

6. The presence of subpleural tubercles does not necessarily mean that they will rupture into the pleural cavity. They do not, therefore, contraindicate pneumolysis, unless tubercles present in adhesions are subject to direct injury by the electrode.

7. The complications after all three procedures are enumerated, with special reference to tuberculous empyema.

8. Comparative statistics indicate that complete pneumolysis was followed by conversion of sputum and closure of cavities in about two-thirds of the procedures and that partial pneumolysis or thoracoscopy accomplished the same results in about one-third of the procedures. The length of time for the closure of cavities and the conversion of sputum increased in these procedures in the following order: complete pneumolysis, partial pneumolysis, and thoracoscopy. The con-

version of sputum occurred about 1 month after the collapse of the cavity.

9. In our entire series of 100 cases, 40 patients had a favorable outcome following all the procedures. The cavities closed, the sputum was converted and there was symptomatic improvement. The average follow-up time was 10 months.

10. If it is generally accepted that 90 per cent of patients with cavitation and restraining adhesions will die without operative intervention, then our statistics indicate that even in far advanced cases partial or complete pneumolysis reduces the mortality considerably.

11. There was a 3 per cent operative mortality and the causes of death are given. The remaining 24 per cent, all of whom had bilateral disease, died from causes not attributed to operation, in an average time of 9 months.

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CONTINUOUS—SERIAL, FRACTIONAL, CONTROLLABLE, INTERMITTENT—SPINAL ANESTHESIA

With Observation on 1000 Cases

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SINCE April 10, 1939, when we gave the first continuous spinal anesthetic, we have administered more than 1,250 entirely satisfactory anesthesias by this method. In this paper we are giving some of our observations and a statistical report on 1,000 cases.

In this series of cases we have used novocain (procaine hydrochloride) as the anesthetic agent. Our choice of this drug has been deliberate since it is the least toxic of all drugs used in producing anesthesia by injection into the subarachnoid space. By the method of spinal anesthesia we employ we are able to give just sufficient dosage to produce anesthesia to the desired level and degree. This anesthesia is maintained as long as necessary by adding subsequent small doses as they are needed. We have thereby changed the method of spinal anesthesia from the "single dose" to the "fractional dose" technique which now places spinal anesthesia in the same category with other anesthesias administered by the continuous or fractional dose method; such as intravenous anesthesia, ether, cyclopropane, nitrous oxide, etc.

Safety and *controllability* are the two things we desire most in spinal anesthesia. Sise has pointed out that the first 30 minutes of spinal anesthesia are the most dangerous. It is during this period that deaths and complications are most likely to occur and especially is this true when a single large dose of a toxic drug is administered. We believe, that by giving much smaller initial doses of the drug, it should increase the safety. When the needle is left in the subarachnoid space the drug can be rapidly recovered by withdrawing a sufficient quantity (5 to 10 cubic centimeters) of cerebrospinal fluid if untoward toxic symptoms develop, especially in those patients who are very sensitive to the drug. The toxic symptoms seen following injection of a drug into the subarachnoid space are not due to the drug that is fixed in the lipoid elements of the sensory and motor synapses producing anesthesia but are due to the absorption of the drug from the cerebrospinal fluid into the systemic (venous) circulation. (This factor will be further emphasized when we deal with spinal anesthesia used in thoracic surgical procedures). The respiratory center is the most vulnerable to attack. When and if toxic symptoms of an alarming character develop, the first thing to do is to withdraw rapidly the cerebrospinal fluid containing the toxic agent. The greatest concentration of the drug is in the vicinity of the point of the needle. The nerves promptly recover from the anesthesia. This observation was first made accidentally when a turned stopcock on the syringe permitted an unintentional escape of cerebrospinal fluid into the syringe with a subsequent loss of anesthesia. This phenomenon has since been confirmed on numerous occasions. Spinal anesthesia is maintained by the drug that is present in the cerebrospinal fluid and when the concentration of this drug falls below a definite level the anesthesia promptly wears off. After anesthesia is established it takes relatively small doses to maintain the anesthesia for any desired length of time. If we are doing serious technical operative procedures and it is important to maintain complete relaxation at all times, we give an additional dose of 50

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milligrams of novocain (5 per cent) solution at the expiration of every 30 minutes. Otherwise, we wait for the initial or previous dose to show signs of wearing off before we give an additional injection.

With a single exception anesthesia was produced to the desired level and degree and the operation was completed under spinal anesthesia. The exception here referred to was a case in which the right middle and lower lobes were being removed for bronchogenic carcinoma and while sensory anesthesia was present up to the level of the hyoid bone, a persistent cough, induced by the incidental tugging on the bronchus, could not be controlled. In this instance cyclopropane was used for this part of the operation. In no other case was a supplementary anesthetic necessary. There were no anesthetic fatalities and no neurological complications. Toxic symptoms were promptly controlled by withdrawal of the drug by rapid aspiration of spinal fluid (3 to 10 cubic centimeters) and by giving inhalations of oxygen.

Some of the disadvantages of the single dose method of spinal anesthesia are (1) failure of the drug to "take" or produce anesthesia to the desired level or degree; (2) the action of the drug wearing off before the operation is completed; and, (3) toxic symptoms or even sudden death following the intraspinal administration of a large dose of a toxic drug. In this series of cases we have eliminated these disadvantages by using this new method of spinal anesthesia.

From the clinical and experimental standpoints, it is generally accepted that procaine hydrochloride is the least toxic of all drugs used to produce spinal anesthesia. Its action is also of the shortest duration. The drugs employed in producing spinal anesthesia, which have a more prolonged action, are also found to be more toxic. There is no reason why any drug or combination of drugs used in producing spinal anesthesia cannot be used by the "fractional" dose or continuous method. It should be more safe to use them by this method than by the single dose technique since the patient would be exposed to smaller amounts of the drug, and because the drug could be recovered by aspiration of a sufficient amount of spinal fluid containing it, should alarming symptoms develop and make this action necessary.

Novocain produces anesthesia promptly when introduced, in sufficient quantity, into the subarachnoid space. We have observed that it takes approximately 90 seconds to relieve pain completely and produce muscular relaxation when it is given in subsequent injections. We feel that each patient is a case unto himself and that each has an individual response to novocain. We have observed a case in which the anesthetic action of novocain disappeared every 15 minutes while doses of 100 milligrams each were being used. We have had anesthesia with 50 milligrams of novocain last for an operation that required 1 hour and 45 minutes. Subsequent injections of 50 milligrams each last approximately 30 minutes, producing both motor relaxation and sensory block. By injecting small doses of novocain (15 to 20 mgm.) into the subarachnoid space we have been able to produce sensory block (anesthesia) without causing motor paralysis. In the case of an elderly woman with a strangulated hernia we produced satisfactory anesthesia with 30 milligrams. We are of the opinion that by using this method of anesthesia it is possible to lower the morbidity and mortality rates, especially in serious and prolonged surgical procedures.

TECHNIQUE

Equipment. Figure 1 illustrates the equipment used:

1. *a*, Indicates the head end of pad used in continuous anesthesia; *b*, the break in the pad for detachment when perineal operations are done; *c and c'*, the break in pad for bending at knees when patient is in Trendelenburg position—as suggested by M. J. Nicholson of the Lahey Clinic; *d*, the position of malleable needle left in subarachnoid space of patient when he is lying on back; *e*, the 30 inches of very small caliber thick walled rubber tubing connecting the 10 cubic centimeter Luer-Lok syringe to malleable needle in patient's spine.

2. Close-up of syringe, stopcock, rubber tubing and needle. *a*, Shows the stopcock connecting the Luer-Lok 10 cubic centimeter syringe and the rubber tubing; *b*, the rubber

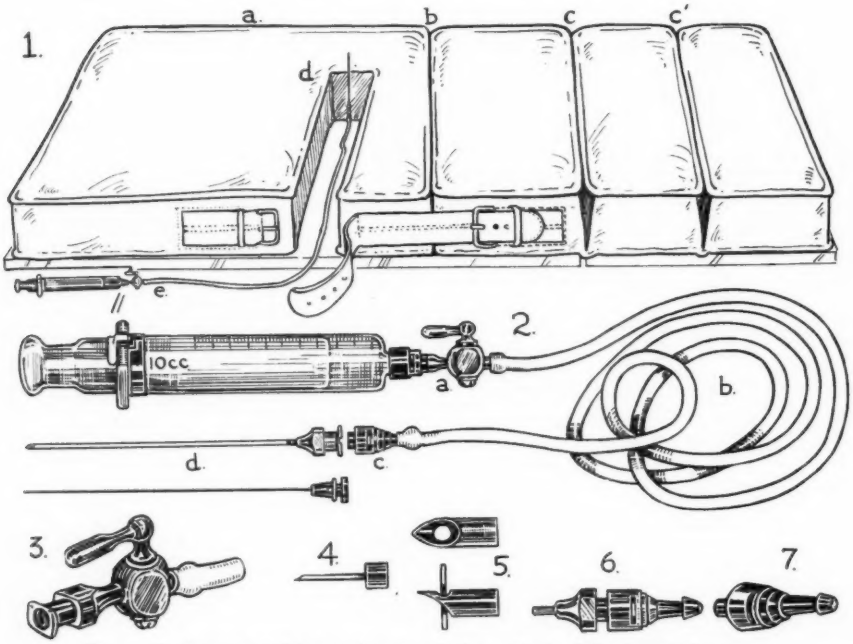

Fig. 1. Equipment used in continuous spinal anesthesia, fully described in text.

tubing—approximately 30 inches; *c*, the Luer-Lok connecting rubber tubing and malleable needle; *d*, malleable needle.

3. Close-up of stopcock.

4. Needle introducer or needle guide used in puncturing the skin.

5. A short bevel with counter opening in the bevel of the malleable needle. This counter opening prevents blockage of the bevel by the meninges, and insures a free flow of spinal fluid.

6. Luer-Lok plug connected to spinal needle to prevent loss of cerebrospinal fluid.

7. Luer-Lok plug.

Administration. In continuous spinal anesthesia we employ a short acting agent, procaine hydrochloride, which is injected in fractional doses as needed during operation. The patient is placed on a specially designed mattress and a very flexible, special alloy, lumbar puncture needle remains in place in the subarachnoid space. This needle is connected to a syringe by means of a 30 inch piece of rubber tubing which is provided with Luer-Lok connections at both ends.

The rubber covered mattress is 5 inches thick, 18 inches wide and 6 feet long (see 1 in Fig. 1). It has a cut-out area 7 inches in length that comes under the lumbar spine when the patient is supine. There is a break in the center of the mattress, so that the part which supports the legs may be detached for perineal operations. Provision has also been made to break the lower part of the mattress to allow the feet to be dropped when a deep Trendelenburg position is desired (Fig. 1, 1*c* and 1*c'*). If an abdominal operation follows the perineal operation, the patient may be pulled back into position and the lower half of the mattress replaced and made secure with straps and buckles (Fig. 1, 1*b*).

The spinal puncture is made with the patient in the left lateral decubitus position so that his back is toward the side of the mattress with the gap in it. The malleable special alloy needles are made in 3 sizes: No. 17, No. 18, and No. 19 gauge. We prefer No. 18 gauge needles. The site selected for spinal puncture depends upon the site of operation—the second or third for upper abdominal procedures,

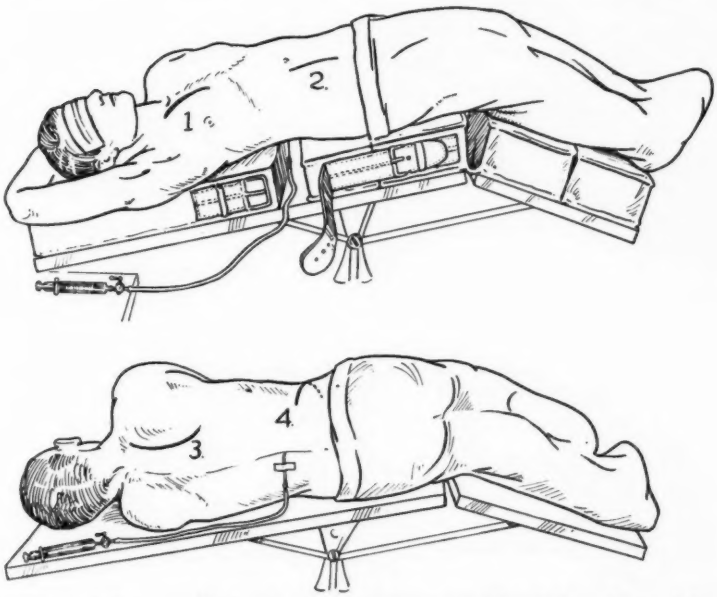

Fig. 2. A diagrammatic drawing demonstrating the position of the patient and the continuous spinal apparatus in place. *1*, *2*, *3*, and *4*, Represent incisions for the surgical procedures in these areas.

the third or fourth for lower abdominal operations, and the fourth or fifth for operations on the perineum, rectum, and lower extremities. A Sise introducer is used to puncture the skin, and, on withdrawal leaves a track for the soft malleable special alloy needle to traverse. When the cerebrospinal fluid escapes from the hub of the needle, a 10 cubic centimeter Luer-Lok syringe is connected with it, and enough fluid is withdrawn to make up a 5 per cent solution. We have 300 and 500 milligram ampuls of novocain. For estimated short operations we use 300 milligrams of novocain, dissolved in 6 cubic centimeters of cerebrospinal fluid. For long operations we dissolve 500 milligrams novocain in 10 cubic centimeters of spinal fluid. The syringe is disconnected and the needle is plugged to prevent a loss of spinal fluid. Generally, 500 milligrams of novocain is dissolved in 10 cubic centimeters of spinal fluid to make a 5 per cent solution, which contains 50 milligrams per cubic centimeter. The syringe with the stopcock attached is connected to one end of the 30 inches of thick walled, small bore, rubber tubing. The stopcock is opened and 2 cubic centimeters of the mixture is forced into the tubing, thus displacing the air and completely filling the tube. Then the stopcock is closed. The Luer-Lok connection at the opposite end of the tubing is securely connected to the needle which was left in the spine. The stopcock is opened and 2 to 3 cubic centimeters of the mixture is introduced into the subarachnoid space and the stopcock is closed.

With the needle left in place, the patient is gently turned on his back so that the needle points downward in the center of the gap in the pad. It should not touch the table or mattress at any time. The patient should be kept in 5 degree Trendelenburg position during the induction period. When the height of anesthesia is tested and the desired level is not obtained in 10 minutes an additional injection, usually of 1 cubic centimeter is made. The height of the anesthesia can be extended and controlled by the following means: position of patient, volumetric dilution of anesthetic agent (barbotage), rate of injection, and total dosage of drug.

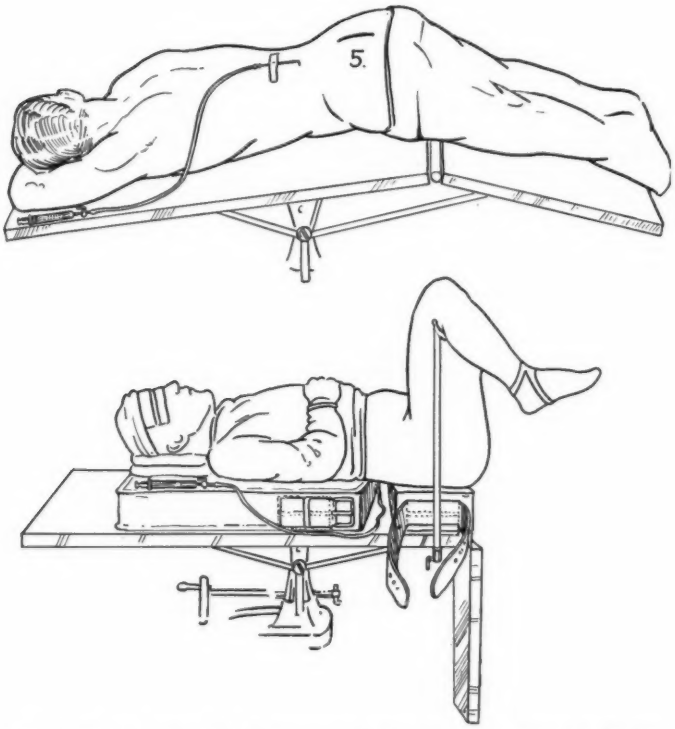

Fig. 3. The patient lying face downward and the spinal needle bent to the side and secured with adhesive. This position used for such operations as excision of the coccyx, and similar operations. The lower drawing shows the lower half of the pad removed and the patient in lithotomy position.

Once anesthesia is obtained, it is easily prolonged by small fractional injections when needed, and we have a setup comparable to the one existing when ether is given by the open drop method or when pentothal sodium is given by the fractional dose intravenous technique. As the anesthesia begins to wear off it is so indicated by the fact that the intestines become less contracted, the abdominal muscles grow more tense, and the patient complains of abdominal discomfort or pain. Just as we would add more ether under similar circumstances to produce relaxation during inhalation anesthesia, when this occurs during continuous spinal anesthesia we give a small additional dose of novocain, usually 50 milligrams. We have noted that it takes approximately 90 seconds for this added dose to exert its full effect. We now give these additional doses, in longer operative procedures, at fairly regular anticipated intervals (usually every 30 to 40 minutes) and are provided with uninterrupted ideal operating conditions throughout the operation.

Preoperative medication. We consider the preoperative medication to be of great importance. On the evening before operation the patient receives 3 grains of nembutal. Three hours before operation the patient is given a second dose of 3 grains of nembutal by mouth. One hour before operation a hypodermic of ¼ grain morphine and 1/100 grain of scopolamine is given. If the sedation is not sufficient, ⅛ grain of morphine is given intravenously or hypodermically as often as is necessary during the operation. By using proper sedation the patients are spared the unpleasant memories sometimes accompanying

such an experience. Most of them sleep throughout the operative period and afterward for many hours.

During long and difficult procedures an intravenous injection of 10 per cent glucose solution is given via a vein in the leg. These patients also receive a blood transfusion at the end of operation if it is indicated. We make an effort to prevent and combat shock rather than wait until its onset before treatment is begun.

ANALYSIS OF CASES

We are presenting a report on the first 1,000 cases in which this method has been used. The operations in this series include 970 below the abdominal diaphragm and 30 above it. In only a single case of the latter group was there a supplementary anesthetic used and that in a case of uncontrolled cough during the course of a pulmonary lobectomy. In this case cyclopropane was used during the stage in which tugging on the bronchus precipitated the cough. Sensory anesthesia in this case was at the level of the hyoid bone. In all of the other cases the operation was begun and finished under spinal anesthesia, and no general or other anesthetizing agent was used.

Age. The average age for this group was 37.2 years. The oldest patient was 83 years old and the youngest was 7 years of age. We did an appendectomy on the latter and a leg amputation on the former. Younger children do not give satisfactory co-operation to permit the extensive use of spinal anesthesia in that age group (under 7 years).

Length of operation. The average length of the operations in this series was 50.4 minutes. A total gastrectomy required 215 minutes (3 hours and 35 minutes. The shortest procedure took only about 2 minutes for the incision and drainage of an abscess. One of our colleagues reported using this method to produce satisfactory anesthesia during the entire course of a gastrectomy requiring 6 hours.

Dosage. For these 1,000 cases the average total dose of novocain was 219.9 milligrams. In the operations done above the diaphragm the dosage was much larger than the general average, being 445 milligrams. This high figure influences the total percentage considerably for it is seen that in the remaining 970 cases the average total dosage was only 181 milligrams of novocain. The average number of injections was 2.4. It is interesting to compare the average total dose of the first 500 cases which was 242 milligrams with that of the second 500 cases which was 198 milligrams. We feel that this reduction in amount of total dose is due to our increased experience. The largest dose given to any one patient was 2,200 milligrams. This patient had had an earlier operation in which she required 1,800 milligrams of novocain to produce anesthesia. This would indicate an individual tolerance and points out, too, that the dose in any given case is *enough*. The smallest dose was 20 milligrams of novocain for amputation of a toe.

We have used various dilutions from 1 per cent to 10 per cent solutions of novocain. We have obtained best results from using a 5 per cent solution of novocain. At times we have used previously prepared solutions of novocain in distilled water and while anesthesia was obtained the results were not always as satisfactory as when the solutions of novocain crystals in spinal fluid were used. In thoracic surgical procedures we generally employ a dilution of 1 to 3 per cent. This will be discussed more completely in a later paper.

Effect on blood pressure. The average systolic blood pressure at the beginning of operation for this series was 125.9 millimeters of mercury. The average systolic pressure at the end of operation was 113.9 millimeters of mercury. This indicates that there was an average fall in systolic blood pressure of only 12 points. The blood pressure was recorded every 5 minutes of the operation. It was noted that soon after the patient received the preliminary injection of ephedrine sulfate and novocain used to anesthetize the skin and support the blood pressure, there was a general elevation of the blood pressure but after the operation was in progress, the pressure had a tendency to become constant or to fall below that at the onset. The average high blood pressure was 129.9. The average low was 103.4. A woman operated upon for a strangulated hernia had a blood pressure of 240 at the beginning and 170 at the end of operation. She received 150 milligrams of novocain in 2

injections. In several instances the blood pressure fell to a systolic of 40 millimeters of mercury. We rarely use vasoconstrictors in these conditions but have found that venoclysis or blood transfusion affords the best relief. Most of these patients leave the operating room in good condition. They have a dry skin and a full pulse of good quality.

Morbidity. Headache. This is a difficult thing to understand and hard to explain. In cases of the most simple nature we have had this complaint. Some patients subjected to longer operations had no subsequent headache. Our incidence of headache after spinal anesthesia is 2.8 per cent, which approximately corresponds to the incidence seen by the former single injection method. We call attention to the fact that we had 150 consecutive cases in which there were no postoperative headaches. In most instances this complaint is relieved by the use of aspirin or by lowering the head of the patient.

Urinary difficulty. There is no greater incidence of urinary retention with this method than with the ordinary method of spinal anesthesia. Our incidence of urinary retention was 3.4 per cent. In some of our plastic or pelvic operations we inserted an indwelling catheter for the first few postoperative days so that these patients do not enter into our statistics.

Pulmonary. There were 34 cases of pulmonary complications, 19 of these were bronchopneumonia, 9 were lobar pneumonia, 4 were atelectasis, and 2 were pulmonary embolism.

Nervous. There were no motor or sensory disturbances, no cranial nerve palsies or other neurological phenomena. A number of these patients have been observed for more than 2 years.

Mortality. There were 47 deaths among this series of 1,000 cases, making the gross mortality of 4.7 per cent. The average time that elapsed between operation and death was 6.9 days. In none of these deaths do we believe that the anesthesia was a contributing factor. Of the 47 who died 24 were suffering with malignant growths. There were 9 deaths from diffuse peritonitis. Among the remaining factors causing death were pulmonary, cardiac, and renal conditions. From several others using this method we are informed of something more than 1,000 additional cases in which continuous spinal anesthesia was used. These added to our series make a known total of more than 2,000 cases. There has not been a death reported from the use of continuous spinal anesthesia.

Table I is an outline of the 1000 cases in this series.

TABLE I.—OUTLINE OF 1,000 CASES DONE UNDER CONTINUOUS SPINAL ANESTHESIA

	Number
Gastrointestinal operations	
Stomach	46
Appendix	285
Intestinal and colon	45
Biliary tract operations	106
Hernia operations	112
Sympathetic nervous system operations	13
Gynecologic operations	
Perineal	38
Abdominoperineal	91
Abdominal	63
Obstetric operations	62
Urologic operations	25
Proctologic operations	40
Cardiovascular operations	3
Thoracic operations	26
Orthopedic operations	40
Miscellaneous operations	5

Classification

	Number	Number	Total
Gastrointestinal operations			376
Stomach operations		46	
Total gastrectomy	4		
Subtotal gastrectomy and appendectomy	19		
Anterior gastroenterostomy	5		
Closure duodenal ulcer, cholecystectomy, and appendectomy	2		
Closure spontaneous rupture of stomach	1		
Resection bleeding gastric ulcer	1		
Cholecystogastrostomy	2		
Biopsy carcinoma of stomach	1		
Biopsy head of pancreas	1		
Subtotal gastrectomy and cholecystectomy	5		
Closure perforated ulcer	4		
Closure perforated gastric carcinoma	1		
Appendix operations		285	
Appendectomy	235		
Appendiceal abscesses and drainage	7		
Appendectomy and excision ovarian cyst	13		
Appendectomy and salpingo-oophorectomy	4		
Appendectomy and uterine suspension	11		

TABLE I.—*Continued*

Classification	Number	Number	Total
Appendectomy and lysis of adhesions	11		
Appendectomy and reduction of torsion of omentum	1		
Appendectomy and excision of varicocele	1		
Intestinal and colon operations		45	
Abdominoperineal resection of rectum 1st stage	4		
Closure of colostomy	4		
Mikulicz resection splenic flexure	3		
Mikulicz resection sigmoid	4		
Resection ileum—intestinal obstruction	2		
Lysis of adhesions and reperitonealization for intestinal obstruction	14		
Incision and drainage subhepatic abscess	1		
Abdominal section—biopsy of liver	4		
Resection sigmoid primary anastomosis	1		
First stage Lahey	2		
Colostomy	3		
Resection ileum for intussusception	1		
Iliotransverse colostomy	2		
Biliary tract operations			106
Cholecystectomy		37	
Cholecystectomy and lysis of adhesions		17	
Cholecystectomy and appendectomy		31	
Cholecystectomy and T-tube drainage of common bile duct		14	
Cholecystogastrostomy and biopsy head of pancreas		2	
Cholecystojejunostomy		1	
Cholecystectomy and hysterectomy		1	
Choledochostomy		1	
Cholecystectomy and oophorectomy		1	
Cholecystectomy and anterior gastroenterostomy		1	
Hernia operations			112
Unilateral inguinal herniorrhaphy		63	
Right inguinal herniorrhaphy and appendectomy		19	
Strangulated inguinal hernia		2	
Bilateral inguinal herniorrhaphy		11	
Femoral herniorrhaphy		5	
Ventral herniorrhaphy		4	
Incisional herniorrhaphy		2	
Inguinal herniorrhaphy—excision varicocele		1	
Umbilical herniorrhaphy and appendectomy		2	
Umbilical herniorrhaphy		1	
Incisional herniorrhaphy, cholecystectomy and appendectomy		1	
Incisional herniorrhaphy and hysterectomy		1	
Sympathetic nervous system operations			13
Presacral neurectomy, uterine suspension and appendectomy		8	
Bilateral lumbar ganglionectomy		3	
Cervical ganglionectomy		2	

TABLE I.—*Continued*

Classification	Number	Number	Total
Gynecologic operations			192
Perineal		38	
Dilatation and curettage, radium	8		
Dilatation and curettage	13		
Induction therapeutic abortion	1		
Vaginal hysterectomy and perineorrhaphy	2		
Fothergill, anterior and posterior colporrhaphy and perineorrhaphy	2		
Plastic repair	11		
Excision carcinoma anterior vaginal wall	1		
Abdominal perineal		91	
Plastic and section	68		
Plastic and appendectomy	11		
Plastic and hysterectomy	2		
Dilatation and curettage, cauterization of cervix, hysterectomy, salpingo-oophorectomy and appendectomy	8		
Plastic and section, hysterectomy and cholecystectomy	1		
Amputation cervix, cholecystectomy	1		
Abdominal		63	
Supravaginal hysterectomy	14		
Unilateral salpingo-oophorectomy	7		
Bilateral salpingo-oophorectomy, appendectomy	2		
Unilateral salpingo-oophorectomy, appendectomy	4		
Hysterectomy, bilateral salpingo-oophorectomy and appendectomy	18		
Excision ovarian cyst and appendectomy	7		
Hysterectomy and appendectomy	4		
Uterine suspension and appendectomy	3		
Anastomosis of left tube	1		
Biopsy carcinoma of uterus	1		
Bilateral oophorectomy and resection 12 inches of ileum	1		
Drainage of pelvic abscess	1		
Obstetrical operations			62
Cesarian sections		41	
Cesarian sections and ligation of tubes		19	
Cesarian section and appendectomy		1	
Cesarian section and incisional herniorrhaphy		1	
Urologic operations			25
Suprapubic prostatectomy		5	
Perinephric abscess		1	
Ureterolithectomy		2	
Nephrectomy		5	
Excision varicocele		3	
Nephrolithectomy		1	
Hydrocele and circumcision		1	
Orchidectomy		1	
Lysis of adhesions obstructing right ureter		1	
Cystotomy		2	
Excision cyst of urachus, appendectomy		1	
Excision of epididymis		1	
Nephropexy		1	

TABLE I.—*Continued*

Classification

	Number	Number	Total
Proctologic operations			40
Hemorrhoidectomy		26	
Excision of fistula in ano		9	
Incision and drainage ischiorectal abscess		2	
Biopsy, fulguration of anorectal tuberculosis		1	
Fulguration of anorectal tuberculosis		2	
Cardiovascular operations			3
Ligation of patent ductus arteriosus		1	
External iliofemoral arteriovenous aneurism		1	
Right femoral embolectomy		1	
Thoracic operations			26
Revision of wound		1	
Anterior thoracoplasty, 1st stage		6	
Posterior thoracoplasty, 1st stage		5	
Posterior thoracoplasty, 2nd stage		6	
Posterior thoracoplasty, 3rd stage		3	
Posterior thoracoplasty, 4th stage		1	
Lobectomy		2	
Pneumonectomy		2	
Orthopedic operations			40
Sequestrectomy, osteomyelitis		1	
Excision of head of metatarsal		1	
Bilateral amputation of hammer toe		2	
Excision internal semilunar cartilage		4	
Excision pilonidal sinus		19	
Excision of benign tumor of leg		6	
Excision of coccyx		2	
Amputation at mid-thigh		5	
Miscellaneous operations			5
Repair of evisceration		2	
Incision and drainage of abscess		2	
Lipectomy and ventral herniorrhapy		1	

SUMMARY

1. We are reporting 1,000 surgical cases in which operation was done under continuous spinal anesthesia.

2. We have discussed the technique employed in the use of this method and have presented some of the important observations in this series.

3. We wish to emphasize the safety and controllability of this method.

4. We feel that the morbidity and mortality can be lowered by the use of continuous spinal anesthesia.

TOTAL VERSUS SUBTOTAL HYSTERECTOMY FOR BENIGN CONDITIONS

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FOR years the question of whether the cervix should be removed along with the fundus in performance of supravaginal hysterectomy has created much discussion. Even among those surgeons who advocate total hysterectomy the technique in performing this operation is noticeably variable and each method has its own adherents who hold certain fixed opinions as to the results.

This paper is based on a group of 2,684 cases observed consecutively at the Mayo Clinic from 1935 to 1939, inclusive, in which operation was performed for benign conditions of the uterus. In 1,920 cases the surgical procedure was total hysterectomy and in 764, subtotal hysterectomy. Further subdivision was made into several classes; the patients who had similar physical hazards—obesity, anemia, and so forth—were placed in separate groups and these groups were analyzed for the occurrence of complications that arose in each. The object of the study was to detect any relation of cause and effect that may exist between certain physical hazards or the type of operation and the nature of postoperative complication. The most reliable figures are those that were obtained after elimination of all cases in which any type of physical disability had been present. In the remaining cases the surgical risk was minimized by the excellent condition of the patients, so that in this group the only known variable was the type of operation performed. Of these 1,497 patients there were 1,034 who had total hysterectomy and 463 who had subtotal hysterectomy.

EVALUATION OF THE TWO TYPES OF OPERATION

The basic reason for different opinions as to the best type of operation when hysterectomy is considered is founded on the possible development of disease in the retained cervical stump subsequent to subtotal hysterectomy. It is true that in some hands few complications occur in the cervical stump after subtotal hysterectomy, whereas in other hands a long list of pathological changes takes place, making removal of the residual stump at the time of operation the procedure of choice. As to the occurrence of carcinoma in the retained cervical stump, we have little to add. During the 5 year period (1935 to 1939 inclusive) in which the two types of operation were performed in the groups cited, carcinoma of the cervix did not arise in any of the 764 cases in which subtotal hysterectomy was performed. Follow-up reports were not received from the patients during the 18 months previous to the writing of this paper and the future cannot be foretold; however, from insurance tables it is known that 2.5 per cent of deaths among women are due to carcinoma of the uterus. The ratio of carcinoma of the cervix to carcinoma of the uterus in cases treated at the Mayo Clinic is roughly 3:1. It is apparent that in all probability carcinoma will develop in the retained cervical stump in approximately 2 per cent of the cases in this group.

Black reported several groups of patients who had carcinoma of the cervix. From 2.1 per cent to 8.1 per cent of the carcinomas had developed in retained cervical stumps after subtotal hysterectomy. Although these figures do not afford a clue to the actual incidence of carcinoma arising in the stump, they do present forcefully the fact that malignant change occurs in the retained cervical stump subsequent to subtotal hysterectomy. Benign tumors so rarely arise in the cervical stump that the possibility of their development hardly justifies removal of the stump on this basis. Among 1,800 cases in which subtotal hysterectomy was performed Hyams observed

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only 2 cases of benign tumors of the cervical stump following the operation.

Rosenow and Benedict (3), in work on certain types of iritis, demonstrated definitely that the cervix is a persistent focus of infection. It has been shown also that a causal relationship exists between infection of the cervix and Hunner's ulcer. Although it cannot be stated that in every case of iritis or of Hunner's ulcer the disease is due to an infected cervical stump, it is known that this relationship can exist and that in certain cases remarkable cures have been obtained by excision of the infected cervix.

We believe that every patient presenting a diseased cervix in association with other uterine conditions requiring hysterectomy should have a total hysterectomy. This belief is based on the fact that 95 per cent of carcinomas of the cervix arise from erosion and chronic cervicitis. Cauterization of the cervix does not as a rule remove all gland-bearing tissue, nor does it remove the epithelium from the portio vaginalis which is frequently the primary focus of cervical cancer. Therefore, as a substitute for total hysterectomy, application of cautery to cervix is a poor second.

Surgical results. To determine which type of operation was more satisfactory from the surgical standpoint we noted all of the cases in which surgical procedure on the cervix or in the vaginal vault was required subsequent to subtotal hysterectomy or to total hysterectomy. In 2 cases in which subtotal hysterectomy had been carried out prolapse developed which required excision of the cervical stump and a plastic vaginal operation. Prolapse of the vaginal vault did not occur in any case in the group in which total hysterectomy had been performed. The type of secondary procedure most commonly required on the cervical stump was the application of cautery for chronic cervicitis. The secondary procedure most commonly employed among the group in which total hysterectomy had been done was removal of a vaginal polyp, in most instances situated at the point where the vaginal wall was everted at the time of the primary surgical operation. In the group of patients, mentioned earlier, who presented the lowest surgical risk, the incidence of secondary surgical procedures after subtotal hysterectomy was almost twice as high as after total hysterectomy (Table I).

Among the 1,920 patients who had been subjected to total hysterectomy, it was surprising that during the 5 year period of observation prolapse of the vaginal vault did not occur. Further to investigate this point we examined the records of all cases in which operation for vaginal prolapse had been performed during the same 5 year period (1935 to 1939 inclusive). In only 1 case had total hysterectomy been performed; there were 23 cases of prolapsed cervical stump. The interesting point about these cases is that in the majority, nearly 10 years elapsed between the original operation and the return for the secondary procedure. On this basis, vaginal prolapse among the group reported in this paper will not become evident for several years. This time element seems reasonable when the normal atrophy, relaxation, and obesity that occur among most women from 40 to 60 years of age are considered. In 20 per cent of the cases of prolapsed cervical stump, the prolapse was evident before surgical intervention and recurred shortly afterward. The results in this small group emphasize the advisability of performing an associated vaginal plastic operation in such cases if relaxation is present at time the uterus is removed.

Postoperative complications. Among the group of patients who were excellent subjects for operation the complications were classified as follows: (1) postoperative intestinal obstruction, (2) postoperative hernias, (3) poorly healed wounds, (4) parotitis, and (5) pulmonary complications. The incidence of each type of complication was about the same after total hysterectomy as after subtotal hysterectomy. There was not any statistically significant difference in incidence of these complications among 1,497 cases in which the only known variable was the type of hysterectomy performed.

The one outstanding exception to the incidence of postoperative complications was observed after total hysterectomy. In 8 cases of 1,034 in which total hysterectomy was performed there developed postoperative bleeding that required active treatment for control. In

TABLE I.—INCIDENCE OF SECONDARY PROCEDURES: CASES OF LEAST RISK

Procedure	Cases	Second operation required	Per cent
Total hysterectomy	1034	12	1.2
Subtotal hysterectomy	463	11	2.38
Total	1497	23	1.5

practically every case the bleeding was from the everted vaginal mucosa. In the 463 cases in which subtotal hysterectomy was performed postoperative hemorrhage did not take place. The vaginal wall is not cut in carrying out subtotal hysterectomy; consequently, the possibility of hemorrhage from this site does not arise.

In a previous paper (4) we stated that the incidence of pulmonary emboli is higher after subtotal hysterectomy than after total hysterectomy. The explanation of this difference probably is related to the engorgement of the lymphatic channels from the retained cervical stump and to the associated secondary thrombosis in the veins of the broad ligament. Similarly, we demonstrated (4) that the incidence of thrombophlebitis is higher after subtotal than after total hysterectomy.

On the other hand we showed (4) that the incidence of urinary complications following total hysterectomy is higher than that following subtotal hysterectomy. This variation is due to the fact that the dissection of the bladder required in total hysterectomy is wider than in subtotal hysterectomy and therefore causes greater trauma and possibly more damage to sympathetic nerve fibers, resulting in temporary urinary retention which necessitates catheterization for relief. The incidence of vesical infection is parallel to the number of catheterizations, and consequently is higher after total hysterectomy than after the subtotal procedure.

In an earlier paper we demonstrated (4) that the mortality rate in the presence of pelvic infection following total hysterectomy is much higher than following subtotal hysterectomy. The reason for this apparent fact is not definitely known.

Type of convalescence. Much has been said regarding convalescence after total or subtotal hysterectomy. The question of which type of operation carries the least postoperative reaction has been argued in both directions. In order to satisfy our own minds on these points we selected 458 consecutive uncomplicated cases in which hysterectomy had been performed during a single year. Three hundred and forty-eight of the patients had total hysterectomy and 110 had subtotal hysterectomy. In each case record was kept as to (1) the highest peak of fever reached postoperatively, (2) the number of days the temperature remained at 100 degrees F. (37.8° C.) or was higher, and (3) the length of the patient's stay in the hospital. In each regard there was a slight, though definite, difference in favor of subtotal hysterectomy. For any given number of the patients who had total hysterectomy, the fever reached a peak from 0.5 to 0.75 degrees F. higher than for the same number who had subtotal hysterectomy. In regard to the duration of fever higher than 100 degrees F. (37.8°C.) recordings in comparable groups revealed that in the cases in which total hysterectomy was done there was roughly a half day more of fever than when subtotal hysterectomy was performed. The postoperative stay in hospital was a third of a day longer for patients who had total hysterectomy than for those who had subtotal.

TABLE II.—DIFFERENCE IN MORTALITY RATES: ENTIRE GROUP

Procedure	Cases	Hospital deaths	Per cent
Total hysterectomy	1920	15	0.78
Subtotal hysterectomy	764	8	1.04
Entire group	2684	23	0.85

The number of cases here presented seems adequate to afford a definite deduction as to the postoperative reaction of patients to these two types of operation. Beyond question, in comparable cases the operation of total abdominal hysterectomy is associated with a sharper and more prolonged reaction than is subtotal hysterectomy.

Mortality. The foregoing statement suggests that the mortality rate should be higher in the group of patients who are subjected to total hysterectomy. An analysis of the hospital deaths, however, does not substantiate this assumption. Table II demonstrates that the mortality rate following total hysterectomy is 0.26 per cent lower than that following

TABLE III.—DIFFERENCE IN MORTALITY RATES: CASES OF LEAST RISK

Procedure	Cases	Hospital deaths	Per cent
Total hysterectomy	1034	2	0.18
Subtotal hysterectomy	463	4	0.86

subtotal hysterectomy. This figure takes on more significance when it is seen that the mortality rate for the entire group is only 0.85 per cent. When only the patients who were excellent subjects for operation are considered, the difference is even more pronounced. Table III indicated a mortality rate 0.68 per cent lower for the group in which total hysterectomy was performed.

Peritonitis remains the cause of death most commonly encountered. Thirteen of the 23 hospital deaths were due to this complication. Four deaths were caused by pulmonary emboli, 2 by bronchopneumonia and 1 each by: (1) acute nephritis, (2) shock, (3) atelectasis, and (4) postoperative hemorrhage.

Nine of the 13 deaths from peritonitis occurred in the group of patients who had total hysterectomy. The remaining 4 followed subtotal hysterectomy. The incidence was practically the same for the two types of procedure, 9 in 1,920, or 0.46 per cent, for the former type and 4 in 764, or 0.52 per cent, for the latter.

From these figures it would seem that neither operation offers a difference in the possibility of subsequent development of fatal peritonitis. However, as we demonstrated previously, among those patients who present evidence of infection at the time of surgical intervention the mortality rate is definitely higher following total hysterectomy than following subtotal hysterectomy. For this group of patients, therefore, the operation of choice is subtotal hysterectomy.

SUMMARY

In a review of 2,684 consecutive cases in which abdominal hysterectomy was performed for benign conditions, analysis was made of the postoperative complications and of the results obtained. Of the 2,684 patients, 1,920 were subjected to total hysterectomy and 764 to subtotal hysterectomy.

Total abdominal hysterectomy is favored by the following considerations: (1) The cervix as a possible source of subsequent malignant change is eliminated. (2) The cervix as a focus of infection is removed completely. (3) A more stable vaginal vault is obtained and secondary operations are obviated. (4)The incidence of postoperative pulmonary emboli and postoperative thrombophlebitis is lower. (5) The mortality rate is lower.

Subtotal hysterectomy also is favored by various considerations: (1) The postoperative reaction of the patient is less marked. (2) The incidence of urinary complication is lower. (3) There is not any danger of secondary hemorrhage from the vaginal vault. (4) In cases in which infection is present at the time of surgical intervention the mortality rate is lower.

CONCLUSIONS

Comparison of the postoperative complications and the results in the two groups of cases furnished the basis for our conclusions.

1. The elimination of the cervix as a source of subsequent trouble and the lower mortality rate associated with its removal far outweigh any known complication that may arise after total abdominal hysterectomy.

2. Except for cases in which infection is present at the time of operation, total hysterectomy apparently is the operation of choice when surgical removal of the uterus for benign conditions is indicated.

3. The secondary hemorrhage from the vaginal vault and the increased urinary complications which follow total hysterectomy usually respond satisfactorily to appropriate treatment.

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A STUDY OF THE MECHANICS OF BILE FLOW

III. Responses to Pharmacological Stimuli

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IN an earlier paper (12) we have described the method of simultaneously observing the effects of those structures we considered most important in controlling the flow of bile. In that communication we also reported our observations on the influence of physiological intravenous solutions upon these structures. In a subsequent report (13) we described the effects of instillation of various solutions into the duodenum. In the present paper we wish to present the results of stimulating the gall bladder, sphincter of Oddi, and the duodenum with pharmacological agents introduced intravenously. The experimental technique is identical to that used in the two reports mentioned.

Adrenalin was injected intravenously fourteen times into 12 dogs; 0.1 cubic centimeter of a 1:1000 solution was the usual dose. The variability in the response of the gall bladder to adrenalin has been recognized in the literature and our results on the effect of adrenalin on the sphincter and duodenum, in addition, illustrate a similar variable effect. In a number of animals the response of the sphincter was diphasic, i.e., an initial decrease of its tone was followed by a secondary rise. In the duodenum the effect was one of a transitory inhibition of activity and decrease in tonus, followed by a rise in tonus and motility concomitant to the secondary rise in sphincteric resistance. The degree of response varied among different dogs, and in some the only effect seen was the rise in sphincteric and duodenal tone. In the latter group the gall bladder showed a relaxation but no change in motility. In one animal the drop in sphincteric resistance far exceeded the subsequent rise above normal and at the same time the gall bladder contracted instead of relaxing as was more commonly observed. Lueth (15) has drawn attention to the fact that the effect of adrenalin on the sphincter varies with dosage.

The use of another member of the adrenalin group, epinine (0.2 c.c. of a 1:100 solution intravenously) gave similar variable results (Fig. 3). With this latter drug the gall bladder showed contractions more frequently than with adrenalin. Ephedrine gave responses in no respect different from those of adrenalin and epinine.

Propradrine hydrochloride injected intravenously in 20 milligram doses gave similar but less marked results in the individual animal. The characteristic rise in blood pressure following intravenous injections of medium doses of adrenalin and epinine was usually followed by a subsequent drop below normal; this secondary drop was absent in the case of ephedrine and propradrine.

The effect of adrenalin was diminished but not abolished by a previous injection of trasentin or of atropine. It may be of significance that the same animal usually responded in a uniform manner to any of these adrenergic drugs used. This would imply that another explanation of the variable responses to injections of sympathomimetic drugs may lie in the individual response to stimulation of the autonomic system.

Houssay and Rubio found that the sympathomimetic drugs relaxed the isolated, perfused gall bladder, adrenalin being more effective than ephedrine. After atropine, these drugs still had the same effect. Other literature is quite contradictory. Some (1) describe contraction of the gall bladder on direct application of adrenalin. Some describe a diphasic (1) or triphasic (27) response with large intravenous doses. Necheles found contraction of the gall bladder in normal unanesthetized dogs (19).

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A preliminary report was read at the meetings of the American Physiological Society, April 19, 1941, Chicago.

Dr. Kozoll, Bernard Portis Research Fellow in Surgery.

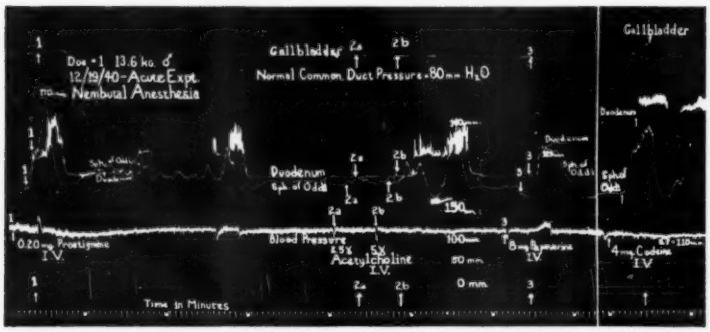

Fig. 1. At *1*, prostigmine, given intravenously, produced an initial simultaneous spasm of the sphincter and duodenum. Subsequently duodenal tone rose steadily, while sphincter tone remained practically normal. At *2a* and *2b*, repeated intravenous doses of acetylcholine, produced slight immediate effects. Thereafter a diphasic relaxation and contractions of the sphincter occurred, independent of a maintained tonic contraction of the duodenum. At *3*, papaverine, *i.v.*, showed a simultaneous rise in the tone of the sphincter and duodenum; however, the sphincter relaxed while elevated duodenal tone persisted. The gall bladder showed an immediate small relaxation. Codeine produced simultaneous immediate spasm of sphincter and duodenum.

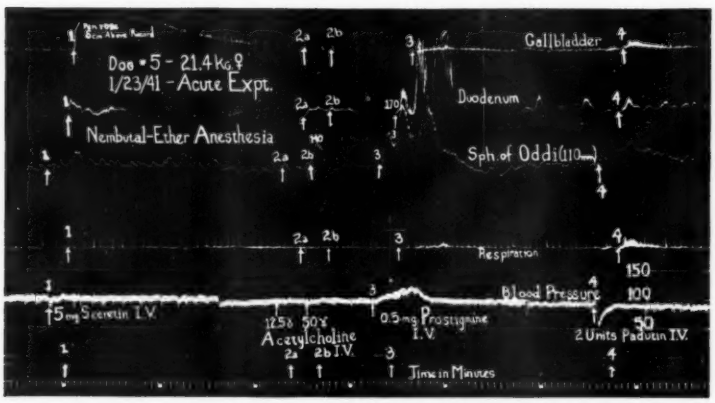

Fig. 2. At *1*, a secretin-cholecystokinin preparation, *i.v.*, produced a marked tonic contraction of the gall bladder which persisted for approximately 30 minutes. An increase in duodenal tone and motility occurred simultaneously, but sphincter pressure was hardly affected. At *2a* and *2b*, acetylcholine, given intravenously, produced relatively small changes in duodenum and sphincter. At *3*, intravenous prostigmine, produced marked recurring simultaneous spasms of sphincter and duodenum. Gall bladder showed only a respiratory effect. At *4*, 2 units of padutin produced a moderate spasm of sphincter, no particular change in duodenum, and a small contraction of the gall bladder.

Acetylcholine was injected in 5 animals in doses varying from 5 to 50 gamma intravenously. In only one instance was there a significant effect. In this case there was a marked lowering of intraductal pressure associated with recurrent episodes of duodenal spasm. The gall bladder showed no response. In all other cases the response was relatively insignificant, except when a dose as large as 50 gamma was given. However, when the injection of acetylcholine was preceded by prostigmine (Fig. 1), it was usually effective in eliciting moderate rises in intraductal pressure and duodenal motility. Lueth (15) described in-

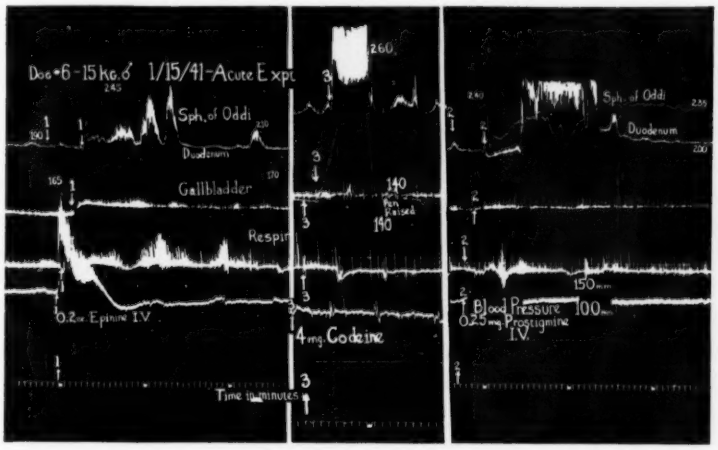

Fig. 3. At *1*, a recurrent diphasic response of the sphincter of epinine, given intravenously, was seen. Note, that a fall of sphincter pressure was followed by a rise above normal. An elevated sphincter pressure persisted even when the duodenum had relaxed from its recurrent spastic contractions. The gall bladder showed a marked prolonged tonic contraction. This animal responded in a similar manner to adrenalin and propradrine. At *2*, intravenous prostigmine, produced several recurring sphincter spasms which preceded and persisted long after the duodenum had relaxed from a prolonged spasm. Gall bladder showed no significant changes. At *3*, intravenous codeine, produced a marked immediate spasm of sphincter and duodenum. No effect on gall bladder.

creases in sphincter pressure and duodenal tone due to acetylcholine. Sandbloom, Voetglin, and Ivy attribute any gall-bladder contractions with this drug to changes in liver volume.

Prostigmine in 0.2 to 0.25 milligram doses intravenously was effective in every case of 12 animals in producing a marked sphincteric and duodenal spasm and usually no effect on the gall bladder (Figs. 1 and 3). Under the influence of prostigmine, we have frequently seen the sphincter relax in the midst of a prolonged duodenal spasm, and vice versa (Figs. 1 and 3). We have had occasion to refer to this independent activity of these two structures under other conditions in our previous publications (12, 13). No significant increase in the tonus or motility of the gall bladder was observed. In one atropinized animal prostigmine was completely without effect (Fig. 4). Our results with this drug are compatible with the reports of others using physostigmine (3, 5, 14).

Pilocarpine 0.5 to 1 milligram intravenously, produced marked gall-bladder contractions and a simultaneous rise in sphincteric pressure and duodenal tone in every one of the 8 cases in which it was used (Fig. 6). A 25 milligram dose of trasentin abruptly abolished the tonic contraction of the gall bladder produced by pilocarpine in one dog. The ability of pilocarpine to contract the gall bladder is generally recognized (3, 11, 14, 22, 27, 29), but its inability to evacuate the gall bladder is attributed to the sphincteric spasm which occurs at the same time (5, 9, 29).

Five milligrams of a secretin-cholecystokinin preparation was injected intravenously 8 times in 7 animals. In each instance an immediate tonic contraction of the gall bladder and duodenum followed (Fig. 2). This is in agreement with previous work (2, 8, 10, 26). After an interval of several minutes an increase in sphincteric resistance occurred; during this interval we believe effective gall-bladder evacuation can occur (Fig. 2). The tonic contraction of the gall bladder was considerable and persisted for 20 or more minutes, long after duodenal or sphincter spasm had subsided. The dose of secretin-cholecys-

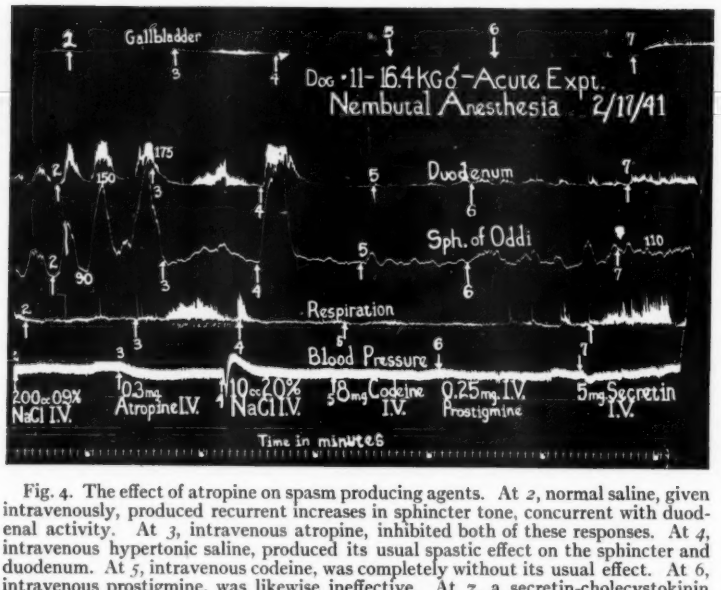

Fig. 4. The effect of atropine on spasm producing agents. At *2*, normal saline, given intravenously, produced recurrent increases in sphincter tone, concurrent with duodenal activity. At *3*, intravenous atropine, inhibited both of these responses. At *4*, intravenous hypertonic saline, produced its usual spastic effect on the sphincter and duodenum. At *5*, intravenous codeine, was completely without its usual effect. At *6*, intravenous prostigmine, was likewise ineffective. At *7*, a secretin-cholecystokinin preparation produced a marked tonic contraction of the gall bladder without a duodenal and sphincter response, probably due to the atropinization.

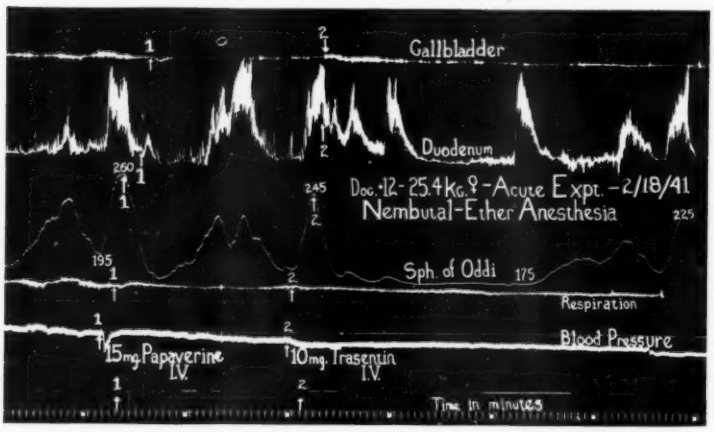

Fig. 5. At *1*, intravenous papaverine produced a precipitous drop in sphincter pressure previously produced by normal saline with gradual return to previous levels. The duodenum was inhibited and the gall bladder relaxed somewhat. At *2*, intravenous trasentin was followed by an immediate drop in sphincter pressure while duodenal tonus and motility were at first unaffected. Gall-bladder tone dropped slightly. The sphincter pressure was maintained at a low level, while later duodenal activity was inhibited for a shorter period of time. Gradually there was a return to previous state of activity.

tokinin used had no significant effect upon blood pressure. Previous administration of atropine or trasentin had little or no influence on the effects of this drug (Figs. 4 and 6).

The response of the sphincter and duodenum to papaverine in 8 to 15 milligram doses, intravenously, showed considerable variation. In 5 of 10 cases there was an initial relaxation followed by a subsequent rise to or above normal (Fig. 5); in others, spasm of sphincter and duodenum were a dominant effect (Fig. 1). In every instance that papaverine had an effect on the gall bladder, it was one of moderate relaxation (Figs. 1 and 5). Papaverine produced relaxation of a tonic contraction of the gall bladder produced by cholecystokinin in 2 dogs. This relaxing effect of papaverine on the gall bladder has been observed by others (9, 18).

Four to 8 milligrams of codeine produced marked increases in sphincteric tone and duodenal peristalsis in every case in which it was employed (Figs. 1 and 3). The effect was immediate and did not appear to influence the gall bladder. Previous injections of atropine and trasentin reduced or abolished the effect of codeine (Figs. 4 and 6). The literature is replete with accounts of the spastic effect of opiates on all smooth muscle (7, 23, 24). Although no specific information is available on the influence of codeine on the gall bladder, a closely related alkaloid morphine is thought to be without really significant effect (8, 14, 17, 27).

Atropine, 0.2 to 0.3 milligram intravenously abolished the tonus rhythm of the sphincter as well as duodenal motility. The depressant action of atropine on intestinal activity is well known (6, 15, 24). The small doses employed of this drug did not actually lower intramural pressure, but rather inhibited the occurrence of spasms. The same doses of the drug were without effect on the gall bladder other than a slight decrease in tonus rhythm.

Various agents, of known ability to produce spasms of the sphincter and duodenum, were given after atropinization with the following results: Atropine was ineffective in abolishing the spasm of the sphincter and duodenum produced by gastric juice introduced into the duodenum, of intravenous adrenalin, and of intravenous hypertonic saline (Fig. 4). The effect of prostigmine (Fig. 4) and of normal saline intravenously (Fig. 4) was abolished and the effect of codeine (Fig. 4) was either

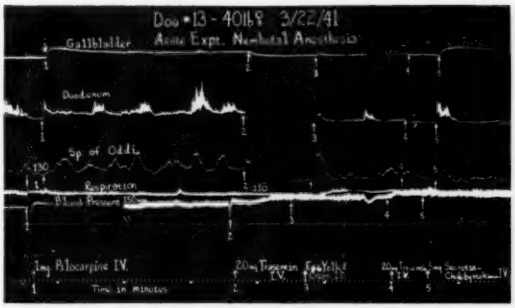

Fig. 6. At *1*, intravenous pilocarpine produced an immediate tonic contraction of the gall bladder of about 20 minutes duration. Simultaneously a moderate increase in the tonus of the duodenum ensued with a similar response of the sphincter after more of an interval than is usual. At *2*, intravenous trasentin, a synthetic antispasmodic, produced a significant relaxation of all three structures. Intraduodenal instillation of a mixture of egg yolk and cream at *3* produces a contraction of all three structures despite the previous antispasmodic medication. Likewise, another injection of trasentin at *4*, did not influence the effect of a secretin-cholecystokinin preparation injected intravenously at *5*.

reduced or completely inhibited. Secretin was capable of producing a moderate gall-bladder contraction following atropinization. Ivy (9) reported that the effect of cholecystokinin on the gall bladder was not prevented by atropine. We were not able to confirm the relaxation of the gall bladder with atropine noted by many workers (9, 10, 11, 14, 16), although we occasionally saw a decreased tonus rhythm; however, we used relatively small doses of atropine.

Trasentin A had similar effects as atropine, in doses of 10 to 25 milligrams intravenously (Figs. 5 and 6). As with atropine, the effects of adrenergic drugs were not influenced, nor was hypertonic saline, intraduodenal instillation of gastric juice, or egg yolk, or secretin-cholecystokinin. Trasentin relaxed a tonic contraction of the gall bladder induced by pilocarpine in one dog. The new trasentin A preparation which was used did not seem to have such pronounced effects on relaxation of the gall bladder as trasentin was reported to have had (21).

Pituitrin was administered intravenously to 3 animals, and in all 3 a moderate gall-bladder contraction occurred before a moderate rise in sphincter pressure and duodenal spasm; the latter followed after an interval of several

minutes. The contraction of the gall bladder following intravenous surgical pituitrin does not compare with that produced by cholecystokinin or pilocarpine. An initial decrease preceding the rise of tone of the sphincter and duodenum described by some (5, 15) was not seen. Gall-bladder contraction with pituitrin has been described by others (8).

Decholin, 0.5 to 1 cubic centimeter, was injected intravenously into 4 dogs, with varying results. There was no characteristic response of the sphincter or duodenum, but the gall bladder relaxed in 3 of the 4 animals used. The use of this drug was associated with a marked increase—about 50 per cent—in the flow of bile collected from the hepatic ducts.

A urinary extract with vasodilator properties, padutin, was investigated. The drug had variable effects on the sphincter and duodenum in a normal state of tone, but appeared to relieve a state of spasm of the sphincter produced by other measures.

Nitroglycerin and amyl nitrite also produced temporary relaxation of the sphincter from a spastic state. Theophylline had no significant effects.

Experiments on human subjects. Patients that had been subjected to cholecystectomy and common duct drainage were utilized after biliary drainage had been established and the patient recovered from the operation. Similar to the procedure of Doubilet and Colp and Walters et al. the common duct was perfused with saline solution and connected to an oil-carbon tetrachloride manometer which accurately indicated the resistance of the sphincter of Oddi to the flow of perfusion. Various drugs were administered by injection, orally, or admixed to the perfusion fluid. It is beyond the scope and extent of this paper to discuss these results in detail, and they will be reported separately (20), but it may be stated that a number of observations on the dog, reported, were corroborated on the human.

ANALYSIS OF STUDY

The most important factor in the emptying of the gall bladder ought to be that of reciprocal innervation of the gall bladder on the one side and sphincter and duodenum on the other. This process has been described as contraction of the gall bladder with simultaneous relaxation of the sphincter of Oddi and duodenum. Whether such a reflex exists or not, it is apparent that emptying of the gall bladder can occur only if during contraction of this organ the sphincter and duodenum do not remain contracted all the time. In other words, if there is no orderly reciprocal innervation, there must be at least temporary periods of relaxation of sphincter and duodenum during contractions of the gall bladder in order to permit a more or less effective emptying of that organ. We have analyzed these possibilities in our experiments, and therefore can answer the above question: The gall bladder may empty either by reciprocal innervation or by contraction of the gall bladder during temporary relaxation of both sphincter and duodenum; either waves of duodenal contractions pass over the sphincter leaving it open during the intervals between waves, or the rhythmic opening and closing of the sphincter continues and emptying occurs in these animals with a more or less quiet duodenum; or, third, both of these possibilities are combined. The occurrence of these combinations can be studied from the illustrations. For instance in Figures 2, 4, and 6, following the administration of secretin-cholecystokinin, a marked gall-bladder contraction occurred, which persisted for 20 or more minutes. Although waves of moderate duodenal contraction are immediately induced, sphincter pressure remains low enough for a long enough interval against which the gall bladder could effectively evacuate.

The experiments here reported demonstrate that emptying of bile through the sphincter of Oddi and the emptying mechanism of the gall bladder depend on a number of processes, the timing and intensity of which are the determining factors. It is also demonstrated that reciprocal innervation of gall bladder and of the duodenum and sphincter of Oddi may occur, but it is not a necessary assumption for the emptying reflex of the gall bladder. It is further evident that a combination of drugs may offer great possibilities for the eventual substitution of the fat meal usually employed in cholecystography. Experiments to answer this question are in progress.

SUMMARY

1. The response of the sphincter of Oddi to drug stimulation can be independent of duodenal activity.

2. The emptying mechanism of the gall bladder and the flow of bile through the sphincter of Oddi depend upon a number of processes, the timing and intensity of which are the determining factors.

3. Reciprocal innervation of the gall bladder, the sphincter of Oddi, and the duodenum may possibly occur, but it is not a necessary assumption for the emptying reflex of the gall bladder.

4. Adrenergic drugs which were employed in this study consisted of epinephrine, epinine, ephedrine, and propradrine; all members of this series produced such variable results that they appeared to offer little clinical application.

5. Cholinergic drugs employed were acetylcholine, prostigmine, and pilocarpine. All of these produce contractions of the sphincter and duodenum, of varying degree, and also contractions of the gall bladder in the case of pilocarpine.

6. Codeine produced subtetanic contractions of the sphincter of Oddi and the duodenum without affecting the gall bladder.

7. Secretin-cholecystokinin produced the most effective contractions for evacuation of the gall bladder, but no reciprocal mechanism was evident.

8. The most effective spasmolytic drugs in our hands were found to be atropine and trasentin.

9. The possibility of a combination of drugs which would produce effective gall-bladder evacuation against a relaxed sphincter of Oddi is suggested as an eventual substitute for the fat meal usually employed in cholecystography.

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APPENDICEAL OBSTRUCTION IN THE NONINFLAMED APPENDIX

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THE primary purpose of this report is to present certain anatomical variations in the appendix, and to suggest a relationship between these variations and disease of the appendix as we know it clinically.

From July 1, 1935, to January 1, 1940, 507 appendices were removed on the Third Surgical Division, Bellevue Hospital, with a diagnosis of appendicitis, either acute or chronic. Of these 314 showed definite signs of inflammation and explained adequately the symptomatology of the patient. One hundred and eighty-nine showed no evidence of active inflammation. The pathological diagnoses in this latter group were: lymphoid hyperplasia, sclerosis, atrophy, and obliteration. There were 4 neurofibromas. No carcinoids were seen. Except for neurofibroma and carcinoid, the terms used are descriptive and do not imply disease. Thus, no clinicopathological interpretation is possible.

A desire to investigate more carefully the noninflammatory group stimulated this study. The material was obtained from three sources: (1) adult organs removed surgically, (2) adult organs removed at autopsy, and (3) fetal and newborn organs removed at autopsy.

Group 1 consisted of 100 consecutive appendices removed on an adult surgical service (12 years and over) with a diagnosis of appendicitis.

Group 2 consisted of 49 appendices removed at autopsy from adults dying of causes other than intraperitoneal disease and who gave no history suggesting previous attacks of appendicitis.

These specimens were received in 20 per cent formaldehyde and allowed to fix for 24 hours or longer. They were then described, measured, and cut serially at 0.5 centimeter intervals. Variations in the thickness of the wall and lumen were noted. The sections were embedded in a single paraffin block in order, cut, and mounted so that consecutive cross-sections appeared on a slide. These were stained with hematoxylin-eosin. In extremely long appendices in which the segments appeared similar, an occasional segment was omitted to facilitate technical work. These slides were divided into two groups: (1) those showing active inflammation, and (2) those showing no evidence of active inflammation. Then the individual sections on each slide were compared for variation in histological structure as well as variation in the relative thickness of wall and lumen.

Seventy-two of the surgical group showed definite evidence of inflammation. The following criteria were used: (1) presence of polymorphonuclear leucocytes in mucosa, submucosa or muscle; and (2) presence of polymorphonuclear eosinophils, lymphocytes, or plasma cells in the muscle layers, with or without fibrosis.

In this group evaluation of histological structure was difficult in some cases because of distortion due to acute inflammation. They were divided into three groups: group 1, architecture completely destroyed, 25 cases; group 2, evidence of pre-existing obstruction, 36 cases; and group 3, no evidence of pre-existing obstruction, 16 cases.

Twenty-eight surgical specimens and 49 specimens removed at autopsy showed no evidence of active inflammation. These were grouped according to their structural variations, as follows: group 1, dilatation of the lumen from the proximal end to the tip; group 2, dilatation of the lumen from the proximal end, variable partial occlusion with lymphoid hyperplasia; group 3, variable partial occlusion with lymph hyperplasia; group 4, uniform atresia of the lumen associated with submucosal thickening; group 5, obliteration of the lumen, partial or complete; group

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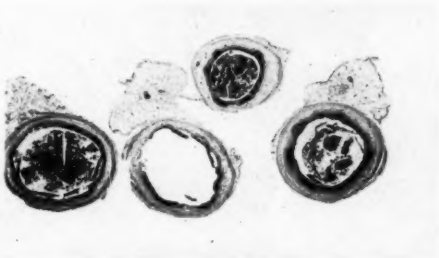

Fig. 1. The lumen is dilated throughout. Mucosal and submucosal layers show atrophy.[1]

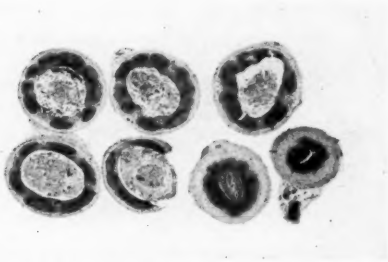

Fig. 2. The lumen is dilated throughout the first 5 segments. There is hyperplasia of the lymphoid tissue. The germinal centers are elongated, their long axis parallel to the circumference of the lumen.

6, appendices showing no evidence of obstruction.

Group 1 presents a uniformly dilated lumen (Fig. 1) from the proximal end to the tip. The changes in the mucosa and submucosa were variable. In some these were quite marked, showing thinning, diminution in number and length of glands with loss of submucosal lymphoid tissue. The muscle layers were thinned. In specimens in which atrophy of the layers was present, the mucosa always presented the most marked change.

In other specimens the wall was thick with hyperplastic lymph follicles having an oblong shape, the long axis being parallel with the circumference of the lumen (Fig. 2).

In Group 2 the proximal segments were dilated. Then there was a variable sized lumen to the tip. This variation usually occurred in the midthird (Fig. 3). The lumen was small, slit-like, the mucosa appearing normal and the lymphoid tissue abundant. Then two or three sections might be encountered with areas of luminal dilatation and mucosal thinning.

Group 3 showed evidence of a variable sized lumen along the appendix (Fig. 4). The first segments showed a narrow lumen. Then the lumen was uniformly dilated to the tip, or it would show several points of narrowing with interdilatation.

Group 4 showed a uniformly small lumen (Fig. 5) with the submucosa markedly thickened due to a large amount of fibrous tissue in the submucosa. The mucosal glands, although decreased in number, were normal in size.

Group 5 showed partial or complete obliteration of the lumen (Fig. 6). The primary change was replacement of mucosa and submucosa by a fibrous core, and one showed a neurofibroma. No conclusive evidence of preexisting inflammation was seen.

[1]The photographs are mounted so that the upper left segment is the base of the appendix and the lower right segment is the tip.

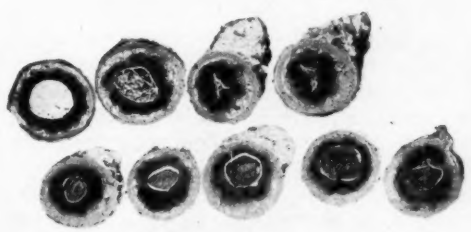

Fig. 3. The lumen is dilated in the 2 proximal segments, slit-like in the third and fourth segments, and increasingly distended in the fifth, sixth, seventh, and eighth segments. Lymphoid hyperplasia is present throughout.

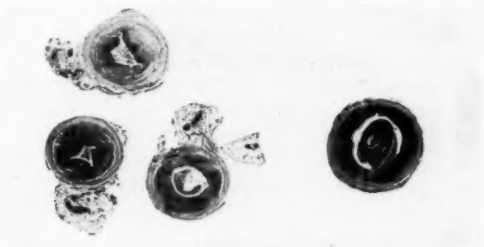

Fig. 4. The lumen is small in the 2 proximal segments with a markedly thickened wall. There is distention in the 2 distal segments. Abundant lymphoid tissue is present in the 3 terminal segments.

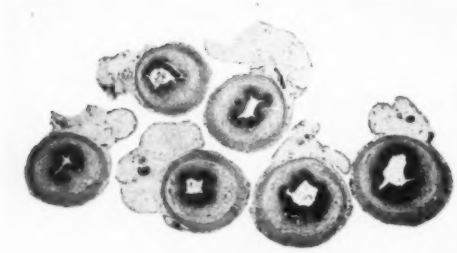

Fig. 5. The lumen is narrow throughout, slit-like in the third segment. The wall is greatly thickened due to the increase in fibrous tissue in the submucosa.

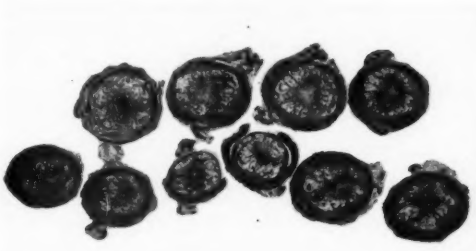

Fig. 6. The lumen is replaced by a fibrous core except in the proximal segment.

Group 6 showed no structural variations from the normal.

When the lumen was dilated either uniformly or irregularly with definite atrophic changes in the layers of the wall (groups 1, 2 and 3), it was thought that these changes were caused by accumulation of fecal material in the lumen with resultant increased intraluminary pressure, this accumulation being due to obstruction or atony of the appendix.

Group 4 showed no atrophic changes but did show a marked variation in the lumen, sufficient to obstruct partially the interchange of fecal material with the caecum.

The appearance of group 5 suggested that it might be an early phase of obliteration of the lumen as seen in group 6.

Groups 2 and 3 show histological evidence of partial obstruction in the wall due to focal lymphoid hyperplasia. We are uncertain whether this is a primary state or whether acute kinks, due to congenital bands, might have prevented the lumen from distending at these points, thus preventing any pressure changes from intraluminary pressure.

Group 1 showed no site of obstruction but definite evidence of increased intraluminary pressure. It was believed that an obstruction could occur at the appendicocecal junction since the appendix enters the cecum at an acute angle in most cases. When the angle is acute, the mucosal fold at the opening (valve of Gerlach) is more prominent.

In these sections it was noted that in specimens in which the lumen was dilated, if lymphoid follicles were present, they were oblong in shape and the long axis of the follicle was parallel to the circumference of the lumen. This was not true if the lumen was not dilated.

Comparing these groups, obstruction occurred in 18 of 28, or 64 per cent, noninflamed specimens removed surgically; in 36 of 52, or 69 per cent, inflamed specimens removed surgically; and in 15 of 49, or 30.6 per cent, specimens removed at autopsy.

In groups 1, 2 and 3, of the noninflamed specimens we believe that dilatation of the proximal segments indicates obstruction at the appendicocecal junction. When there was evidence of obstruction along the appendix at one or more points, the structural variation was a comparative one. While the lymphoid tissue was comparatively abundant and hyperplastic in relation to adjacent dilated segments, actually the mucosa and lymphoid tissue in many cases were normal. We, therefore, believed that extrinsic bands with acute kinks rather than true focal lymphoid hyperplasia may have been responsible for this picture.

We are not prepared to say whether lymphoid hyperplasia *per se* may produce appendiceal obstruction.

By this method of pathological examination we are of the opinion that the pathologist can make a diagnosis of appendiceal obstruction.

The third group of appendices studied consisted of 25 appendicocecal regions removed from stillborn infants and newborn babies which had died. A representative group is shown in drawings (Fig. 7) illustrating the marked variations in position and the presence

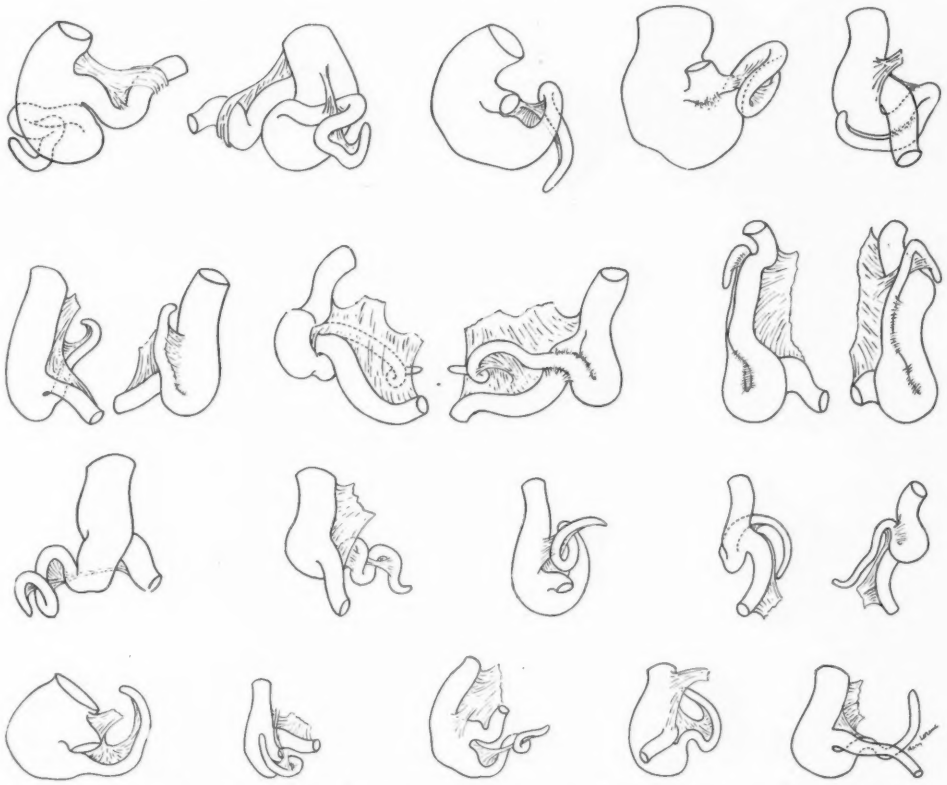

Fig. 7. Drawing of 16 consecutive specimens removed at necropsy. Numbers 1, 5, 6, 7, and 11 show both anterior and posterior views.

of numerous congenital bands causing distortion of the appendix. The appendix was free of bands in only 7 cases. The variations seen here represent almost every type encountered surgically and are presented to emphasize the extreme distortion at birth.

The rôle of obstruction in the etiology of acute appendicitis has long been recognized (5, 7, 11, 12, 13, 14, 15, 16). However, when one peruses the literature on "chronic appendicitis," evaluation becomes extremely difficult because there is no uniform classification which is followed by the clinician and the pathologist.

The term "chronic appendicitis" as generally used has ceased to be a disease entity, but rather a "catch-all" for those cases not showing active inflammation.

In the pathological department at Bellevue Hospital the following classification has been used:

1. Inflammatory
   - acute
   - chronic
     - nonspecific
     - specific
2. Non-inflammatory
   - obstructed with
     - lymphoid hyperplasia
     - sclerosis
     - atrophy, etc.
   - nonobstructed
     - lymphoid hyperplasia
     - sclerosis
     - atrophy, etc.
3. Neoplastic
   - benign
     - carcinoid
     - neurofibroma, etc.
   - malignant—carcinoma, etc.

The term chronic appendicitis is used only when signs of active chronic inflammation are

present. This represents less than 5 per cent of all appendices examined.

Many explanations have been given for the cause of pain in the noninflamed appendix. Barss, in 1918, reported 7 cases of appendiceal disease in children all cured by appendectomy, in which the pathological diagnosis was lymphoid hyperplasia.

Symmers reported 20 cases with similar pathological changes and symptoms simulating those of mild appendicitis, with cures following appendectomy.

Follow-up records show that between 50 and 80 per cent of the patients in this general group operated upon are cured or markedly improved, yet both surgeon and pathologist have been unable to distinguish the offending appendices from those which did not give symptoms.

Since histological evidence of disease is lacking, one is forced to turn to disturbances in function for an explanation of the symptoms.

In *Human Physiology* by Flint, 1892, this statement appears: "The function of the appendix is unknown." Certain recent physiological textbooks fail to mention the organ. Dufor (10) in 1890 advanced the theory that the appendix plays a great part in provoking a desire for defecation, independent of other reflexes involved in the act. Adami and McCrae (10) in 1914 stated: "It is the appendix that is the hydrostatic agent initiating peristalsis in the large gut." These views have not been widely accepted and Flint's statement still stands: "The function of the appendix is unknown."

Although no useful function has been established, we do know that it functions as part of the large bowel; that it is capable of filling and emptying, and that the peristaltic action is similar to that of the large bowel (13).

Anatomically, the appendix vermiformis must be considered as an undeveloped cecum. Embryologically, the appendix is a retrogressive organ, having a relatively higher development in the fetus than in the infant, and must be considered merely as the distal portion of the cecum (7).

Differentiation between cecum and appendix starts about the seventh week and continues to birth when the comparative diameters are 1:4; at 8 years it is 1:6 or 7, and in the adult the ratio is 1:8 or more. One would, therefore, consider comparative retrogression not complete until puberty (7).

The relative location of the appendix is the most variable of any organ in the peritoneal cavity. The location depends on the point of origin from the cecum and varies, first, according to the direction of the cecal pouch, and, second, according to the presence of peritoneal bands which persist following complete rotation of the large bowel.

The appendix is found free of congenital peritoneal bands and entering the cecum at a right angle in about one-third of the cases. The angle at which the appendix enters the cecum varies between 10 and 90 degrees.

The clinical syndrome with which the obstructed appendix is associated is well known. Pain in the right lower quadrant is the one constant symptom, steady or intermittent, frequently associated with anorexia, nausea, and occasional vomiting. The patients are frequently constipated. The only constant sign is tenderness in the right lower quadrant centering over McBurney's point, usually associated with skin hyperesthesia (8). Evidence of active inflammation is lacking. The temperature is normal and the blood count not elevated.

Can the appendix give these symptoms and signs without showing any evidence of inflammation? We believe it can, and does.

It has been shown (8) that distention of the lumen of a normal appendix will give epigastric pain, nausea and pain in the right lower quadrant associated with persistent skin hyperesthesia. This was done through appendicostomies. Therefore, it is reasonable to assume that increased intraluminary pressure due to natural causes can give the same clinical symptoms and signs.

The appendix is a tube, blind at one end and lined with intestinal mucosa capable of secretion and absorption. It opens into the cecum. Intestinal contents reach the cecum in a fluid state, some entering the appendix. Dehydration occurs, and any variation in the diameter of the lumen will favor stasis and accumulation of fecal material. This process,

we believe, will cause distention of the lumen with resultant changes in the mucosa which can be demonstrated histologically by the method of examination herein described.

Anatomically, three methods of obstruction are possible: (1) kinking at the appendicocecal junction, (2) kinking along the length of the appendix due to peritoneal bands, and (3) intra-appendiceal stenosis due to lymphoid hyperplasia or fibrosis.

The point of origin of the appendix from the cecum varies according to the direction of the cecal pouch, and the appendicocecal angle is dependent on the position and development of the peritoneal bands which, in turn, depend on the ultimate position of the large bowel.

Intrinsic obstruction occurs due to variations in the thickness and structure of the wall with consequent encroachment on the lumen.

The first two causes of obstruction, namely, an acute appendicocecal angle and kinking due to peritoneal bands, will be seen only by the surgeon, and in writing up the operation, these details are frequently omitted. Consequently, this information does not reach the pathologist. However, the third cause, namely, intrinsic obstruction, can be seen by the pathologist, but unless the specimen is studied carefully, evidence for intrinsic obstruction may not be recognized.

SUMMARY AND CONCLUSIONS

1. Histological criteria for diagnosing appendiceal obstruction are submitted.

2. Appendiceal obstruction was demonstrated in 18 of 28, or 64 per cent, noninflamed specimens removed surgically; in 36 of 52, or 69 per cent, inflamed specimens removed surgically; and in 15 of 49, or 30.6 per cent, specimens removed at autopsy.

3. This obstruction is believed to be mechanical rather than inflammatory. The etiological factors for obstruction are present at birth.

4. An obstructed appendix may give symptoms without the presence of inflammation.

5 An obstructed appendix definitely predisposes to acute appendicitis.

6. Appendiceal obstruction may exist without giving signs or symptoms.

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SUBACUTE STREPTOCOCCUS VIRIDANS SEPTICEMIA CURED BY EXCISION OF AN INFECTED TRAUMATIC ARTERIOVENOUS ANEURYSM

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THE rarity of coexisting, *acquired* arteriovenous aneurysm and subacute Streptococcus viridans septicemia, is indicated by the fact that up to the present time only 10 such cases have been recorded in the literature. For purposes of classification, they may be divided into two main groups.

The first group consists of cases in which the septicemia precedes, and is responsible for, the formation of the aneurysm. Such a sequence sometimes is observed in subacute bacterial endocarditis, of which mycotic arteriovenous aneurysm may be a late complication. Cases have been reported by Masbrenier, Simmonds, Libman, and Floyd.

The second group consists of cases in which arteriovenous aneurysm is the primary condition, and subacute bacterial septicemia the complication. Primary arteriovenous aneurysms (and fistulas) may be either *congenital* or *acquired*. Among the better known congenital arteriovenous communications (fistulas) may be mentioned patent ductus arteriosus, patent interauricular septum, and patent interventricular septum. Acquired, primary arteriovenous communications (aneurysms) are exclusively traumatic in origin and most commonly are due to gunshot or stab wounds.

Should a patient with an arteriovenous communication of either the congenital or acquired variety develop a transient bacteriemia from some extraneous source, organisms may lodge upon the intimal lining of the arteriovenous lesion. Under such circumstances, vegetations may develop locally; thus there is established a new infective focus from which organisms are shed into the blood stream more or less continuously. When these organisms are of low virulence, the patient suffers from a condition termed "subacute bacterial septicemia." The organism most commonly involved in the latter is the Streptococcus viridans.

The frequency with which subacute Streptococcus viridans infection develops at the site of congenital arteriovenous communications, especially those located within the heart, is well known, and many such cases have been collected by Abbott. The superimposition of similar infection upon acquired arteriovenous communications (aneurysms), although observed less commonly, has been reported by Bretschneider, Walz, Gravier, Porter and Williams, Hamman and Rienhoff, and Leaman. When subacute Streptococcus viridans infection develops at the site of an acquired or congenital arteriovenous communication and organisms continue to be shed into the blood stream, new infective lesions may develop at distant points. One of the most common sites for such secondary localization is upon the endocardium and cardiac valves. When this occurs, the fresh cardiac lesions constitute additional infective foci which themselves are capable of perpetuating the sepsis.

Although arteriovenous communication existing in combination with subacute Streptococcus viridans septicemia formerly was considered to be of interest only to the pathologist and internist, it recently has attracted the attention of the surgeon also. This interest was initiated in 1935 by the report of Hamman and Rienhoff of the first case in which cure of subacute Streptococcus viridans septicemia followed excision of an infected, acquired[1]

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[1]The first surgical cure of subacute Streptococcus viridans septicemia superimposed upon a congenital arteriovenous fistula, (patent ductus arteriosus) reported by Touroff, Vesell in 1940.

arteriovenous aneurysm of the right external iliac artery and vein. These authors emphasized that surgical excision of an infected arteriovenous aneurysm is futile in cases in which vegetations coexist in the heart. For under such circumstances, even though the aneurysm is removed completely, the cardiac vegetations will continue to act as a focus for perpetuation of the sepsis. Thus, operation is contraindicated in cases of mycotic arteriovenous aneurysm occurring as a complication of subacute bacterial endocarditis. For the same reason, operative treatment also is contraindicated in cases of infected, primary arteriovenous aneurysm in which the cardiac valves have become involved secondarily. Accordingly, the only cases which remain amenable to surgical treatment are those of infected, primary arteriovenous aneurysm in which infection has remained confined exclusively to the local site. Under the latter circumstances, local excision of the aneurysm may result in cure.

Since the report of Hamman and Rienhoff, no other instance of cure of subacute Streptococcus viridans septicemia following excision of an infected arteriovenous aneurysm has been recorded in the literature. It therefore appears warranted to report a second successful case in detail.

REPORT OF CASE

R.W., a native born white male aged 26 years, single and a clerk, was admitted to the consultation service of The Mount Sinai Hospital on February 2, 1941, because of fever, malaise, and progressive weakness of approximately 1½ years' duration. During childhood he had had measles, pertussis, and scarlet fever, without sequelae. The surgical history included a bilateral inguinal hernioplasty performed at the age of 5, and a tonsillectomy performed at the age of 7 years.

On entering high school at the age of 14, he was examined by a physician and, because of "frail constitution," was advised to abstain from strenuous athletics. No evidence of any cardiac abnormality was present at the time. Despite the advice of his physician, he participated actively in athletics, including bicycle riding, running, and swimming, without manifesting unusual distress or shortness of breath.

At the age of 17 years—9 years before the present admission—the patient suffered an accidental through-and-through gunshot wound of the left thigh. Although bleeding was profuse, he responded well to treatment and was discharged from a local hospital, symptom free and with the wounds practically healed, at the end of 1 week. Shortly thereafter, he became aware of a peculiar "buzzing sensation" in the thigh. Because this was not associated with other obvious abnormalities, he considered it to be of no importance and failed to mention it when the history was first taken. About a year after the accident he began to suffer from fatigue and dyspnea on exertion. A diagnosis of "chronic heart disease" was made by the patient's physician at the time, but the nature of the cardiac abnormality and its relationship to the previous injury of the thigh apparently was not recognized. He was told however, that his blood pressure was 148/58, and his pulse rate 122. During the next 6 years he continued his activity as a student and then as a clerk, the symptoms of weakness, dyspnea on exertion, and cardiac palpitation becoming increasingly severe.

About 2 years prior to admission to the consultation service, a decayed molar tooth was extracted and the root canal of an adjoining devitalized tooth was filled. Soon thereafter he became acutely ill, with fever and malaise. Loss of weight, strength, and appetite, followed shortly. All of these symptoms, in addition to the pre-existing dyspnea and palpitation, continued with remissions and exacerbations during the next 8 months. About 1½ years prior to admission he suffered an attack of severe left sided pleuritic pain associated with productive cough, but without hemoptysis. Evening rises of temperature to 103 degrees F. and drenching sweats, then began. These symptoms at first caused only periodic confinement to bed, but during the 3 months prior to admission the fever, sweats, and weakness, became so severe that he was bedridden most of the time. During the last month he suffered another attack of left-sided pleuritic pain and three shaking chills each lasting about 20 minutes.

During the year preceding admission he had received large doses of sulfanilamide; and during the last 3 months he had been kept continuously on sulfapyridine therapy.

Examination. The patient first came under the observation of one of us (H.L.) in the consultation service, February 15, 1941. At that time examination disclosed a thin, pale, sweating, somewhat dyspneic young man who appeared acutely and chronically ill. The temperature was 102 degrees F., pulse rate 126, and respiratory rate 22.

A summary of the essential findings follows: Arterial pulsations were distinctly visible in the vessels of the optic fundi. Forceful pulsations were present in the suprasternal and subclavicular areas, and harsh murmurs were noted over the carotid and subclavian arteries. Cardiac action was regular, the apical rate being 126 per minute. The heart was moderately enlarged to the left on percussion; diffuse forceful pulsations being noted in the fourth and fifth intercostal spaces outside the midclavicular line. The first sound here was loud and booming. The second pulmonic sound was louder than the

Fig. 1. Preoperative roentgenogram of chest. Note enlargement of heart to the left and pulmonary vascular congestion.

second aortic sound. Over the apex and pulmonic area, short, soft, high pitched, blowing systolic murmurs were present. All pulses were of the collapsing (Corrigan) type. The arteries of both lower extremities pulsated freely, the pulsations of the vessels on the left being more forceful than those on the right.

Small, almost invisible, scars were present over the lateral and medial aspects of the midportion of the left thigh. At the same level, a plum sized expansile mass, embedded within the muscles close to the inner aspect, was palpable. Over this mass, a coarse thrill and a harsh to-and-fro "machinery" murmur were readily audible. The left common femoral artery was obviously enlarged on palpation and could be seen to pulsate very vigorously. The to-and-fro murmur in the thigh could be heard down to the knee and over the great vessels of *both* legs. The left thigh, leg, and foot were warmer than the right; the diameter of the left thigh was greater than that of the right. The superficial veins of the left leg and foot were prominent.

The liver was palpable for a distance of three fingerbreadths, and the spleen for a distance of four fingerbreadths, below the costal margin. No petechiae, Osler nodes, or Janeway lesions were noted. The fingers were clubbed slightly and capillary pulsation of the nail beds was increased.

The blood pressure in the right arm was 132/70, in the left arm 124/60, in the right thigh 160/70, and in the left thigh 180/0. On firm compression of the pulsating mass in the left thigh, the pulse rate decreased from 112 to 92 and the blood pressure in the right and left arms rose to 138/80, and 132/74, respectively. Oscillometric readings at the right thigh, calf, and ankle were 3¾, 2½, and 1¾, respectively; at the same levels on the left they were 20, 4¼ and 1½.

Laboratory data. A teleoroentgenogram revealed enlargement of the heart to the left and the presence of pulmonary vascular congestion (Fig. 1). On fluoroscopy the left ventricle appeared dilated. The left auricle was not enlarged, and the general configuration of the heart was not that usually noted with valvular disease. The electrocardiogram revealed sinus tachycardia, the rate being 105 per minute. Right axis deviation was present. RT_2 and RT_3 were depressed slightly and T_3 inverted, the tracing suggesting either right ventricular hypertrophy or a vertically placed heart. Upon compression of the left femoral artery, the rate slowed from 105 to 90 per minute, RT_3 became isoelectric and T_3 upright. Upon release of compression, the rate returned to 105, and RT_3 and T_3 assumed their original abnormality. The phonocardiogram revealed a systolic murmur and a short, early, diastolic murmur at the pulmonic area. The cardiac output was 7.2 liters per minute and fell to 5.5 liters upon compression of the left common femoral artery.

X-ray examination of the abdomen revealed marked enlargement of the liver and spleen. X-ray examination of the lower extremities revealed a small irregular area of calcification in the midportion of the left thigh, mesial to the shaft of the femur. The specific gravity of the urine ranged up to 1030. Albumin and dextrose were absent. The microscopic examinations were essentially normal. The blood contained 4,850,000 red cells per cubic millimeter. The hemoglobin content was 62 per cent. There were 9,000 white cells, of which 70 per cent were segmented polymorphonuclear leucocytes, 12 per cent nonsegmented polymorphonuclear leucocytes, 16 per cent lymphocytes, and 2 per cent monocytes. The color index was .7. The smear revealed achromia, polychromasia, and anisocytosis. The erythrocyte sedimentation rate was 20 minutes (markedly accelerated). The Wassermann and Kahn tests gave negative results. The blood agglutination reactions for Bacillus abortus and Bacillus melitensis were negative. Blood cultures on two occasions yielded Streptococcus viridans (alpha) 5 colonies and 1 colony per cubic centimeter, respectively.

For the sake of clarity, the history and laboratory data have been presented in sequential order. Actually, the complete history was elicited with difficulty and it was not until all the details finally were learned that appropriate clinical and laboratory investigations were carried out. For example, when first questioned the patient omitted entirely the history of gunshot wound of the thigh. In view of the negative past history of rheumatic fever and cardiac symptoms during

childhood, and the absence of evidence of valvular lesions and congenital cardiac defects on physical examination, the cause of the cardiac enlargement and high pulse pressure at first was not clear. After the blood culture had been reported positive for Streptococcus viridans, the absence of evidence of cardiac valvular lesions and congenital defects suggested that the patient was *not* suffering from endocarditis. Accordingly, the focus of infection was sought elsewhere. On noting the small scars and the pulsating mass, bruit, and thrill, in the left thigh, the patient was asked whether he had ever been shot or stabbed in that region. When he answered in the affirmative, the diagnosis of arteriovenous aneurysm with superimposed Streptococcus viridans infection was made, and appropriate studies to corroborate the diagnosis were begun. These investigations, which already have been described, established the existence of a large arteriovenous shunt in the left thigh and the presence of Streptococcus viridans in the blood stream. In addition, the studies failed to demonstrate the presence of cardiac valvular lesions, and accordingly the arteriovenous aneurysm appeared to be the most likely focus for the continuing sepsis. Under the circumstances, an attempt at wide surgical removal of the lesion appeared warranted, especially in view of the failure of intensive chemotherapy to result in cure prior to admission to the hospital. On February 17, 1941, the patient was admitted to the surgical service of Dr. Harold Neuhof, where investigative studies were completed and a transfusion was administered.

Operation. On February 18, 1941, an operation was performed (by A.S.W.T.), under nitrous oxide anesthesia. An incision was made over the freely pulsating, enlarged left common femoral artery, just below Poupart's ligament, and carried downward over the approximate course of the femoral triangle and Hunter's canal for a distance of about 8 inches. On exposure, the common femoral artery and vein measured approximately ¾ inch and 1 inch in diameter, respectively; a coarse thrill was palpable over both vessels. The superficial femoral artery and vein next were exposed to a point below the level of the old gunshot wounds, without encountering any abnormality other than dilatation of both vessels and the presence of numerous, engorged venous tributaries. Since the pulsating mass still

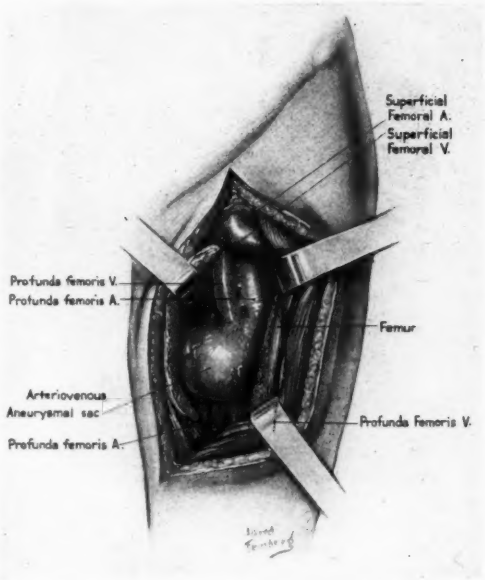

Fig. 2. Schematic drawing of findings at operation. Note great enlargement of the superficial and deep femoral vessels, especially the latter. Collateral vessels covering aneurysm are not shown. Lower and lateral portions of sac lie behind the femur. Note great enlargement of deep femoral vein to form lower portion of aneurysm. Also note small size of deep femoral artery distal to the aneurysm.

was readily palpable within the substance of the adductor muscles, the region about the bifurcation of the common femoral artery next was exposed, and the profunda femoris traced downward by freely dividing the overlying adductor muscles. This vessel and its accompanying vein, at once were noted to be widely dilated. A coarse thrill was palpable over both. As the dissection was carried downward, the vessels were found to be firmly agglutinated to one another and to the surrounding structures by firm scar tissue apparently resulting from old hemorrhage. Gradually the vessels were traced into a freely pulsating arteriovenous aneurysm which lay imbedded in extremely dense, almost cartilaginous, fibrous tissue, mesial to the shaft of the femur and on a plane posterior to the linea aspera.

The aneurysmal sac measured approximately 2 inches by 2 inches. Mesial to it, a communicating thin walled accessory sac measuring roughly 2 inches by 1½ inches was present (Fig. 2). After prolonged dissection, the entire lesion and the four major vascular channels entering and leaving it were freed from the adjacent femur and surrounding scar tissue. The lower portion of the sac was found to extend behind the femur, thus making its exposure in this region quite difficult. Above the aneurysm, the deep

Fig. 3. Interior of excised specimen. Probe passed through proximal artery enters aneurysm from above. Proximal vein is completely obliterated by scar tissue. Lower probe enters aneurysmal sac through the distal artery. Note that the distal vein is widely dilated and, extending downward from the point of hourglass constriction, forms the lower half of the aneurysm. Diverticula (false aneurysms) are present in upper half of sac. Note particularly the scattered vegetations within the interior of the upper half of the sac and the large triangular vegetation within the lower half of the sac. Smears taken from these vegetations revealed large numbers of streptococci, which on culture were reported as Streptococcus viridans.

femoral artery and vein were markedly dilated. Below the aneurysm, the deep femoral vein was found to be the site of enormous fusiform dilatation; the deep femoral artery was of very small caliber. Numerous collateral vessels, both arterles and veins, entered the main sac. The accessory sac was quite free of collaterals and apparently represented a false aneurysm—the result of a hematoma formed at the time of the original injury.

The profunda femoris artery and vein, above the aneurysm, were doubly ligated with heavy silk thread, and divided. All collateral vessels, entering and leaving the sac, also were ligated and divided. Finally the two main vessels below, were ligated and divided, and the entire lesion was removed *en masse*.

Oozing from the dead space within the adductor muscles was controlled by a temporary packing, and the wound closed by loosely approximating the deep fascia of the thigh. The skin was closed with clips. No drainage was employed. A transfusion of 500 cubic centimeters of citrated blood was administered at the conclusion of the operation.

Description of specimen. "The specimen consists of a shrunken arteriovenous aneurysm received in fixative which, in the opened state, measures 7.5 by 6 cm. in its largest diameters. The artery proximal to the aneurysm, measures 4 cm. in length. Its walls appear thin and elastic. The proximal vein is 2 cm. long and is entirely obliterated by dense fibrous tissue. The proximal vessels open into a multilocular cavity, lined by endothelium. The distal artery measures 3 cm. in length and is patent. The distal vein, which is approximately 3 cm. long, is the site of a fusiform dilatation measuring 4 cm. across when opened. At the ostium of the distal vein there is a constriction, below which the enlargement of the distal vein takes place. Between the ostia of the arterial and venous channels, a flat but definite ridge is present. Thus, the opened specimen assumes an hour glass appearance. Connected with the true aneurysmal sac there are 2 diverticula (false aneurysms), each 1 cm. in length. A third diverticulum, the size of a large hazel nut, appears to be obliterated by a thrombus the surface of which is covered by endothelium. Red and gray irregular vegetations, varying in size from the head of a pin to a pea, stud the saccular portion of the aneurysm. The more fusiform portion, formed by the dilated proximal portion of the distal vein, is the site of a large, flat, triangular, organizing grayish red vegetation. The interior of the fusiform portion of the aneurysm presents many sclerotic plaques. The outside of this portion of the aneurysm also presents a calcific plaque. Flat, sclerotic plaques also are present within the wall of the specimen" (Fig. 3). (It is of interest to note that these calcific masses were discernible on preoperative x-ray examination of the left thigh.)

Microscopic report. "Arteriovenous aneurysm showing subacute bacterial endovasculitis (numerous gram-positive cocci are found within the vegetations)."

Bacteriological report. Culture of vegetations which were obtained from within the arteriovenous aneurysm yields a heavy growth of the Streptococcus viridans.

Postoperative course. The patient's immediate reaction to operation was extremely satisfactory. By the third postoperative day, striking improvement in the general appearance and condition was noted. At that time the cardiac murmurs were almost inaudible; the pulse rate was considerably slower and had lost its collapsing character. The highest postoperative temperature was 101.6 degrees F. on the second day. Thereafter it receded progressively and was normal by the 8th postoperative day. The wound was healed by primary union in 6 days; and 2 days later the patient was permitted out of bed. By the 10th postoperative day, the systolic murmur at the apex had disappeared A short, harsh, diastolic murmur was heard over the pulmonic area, only on complete inspiration. The bruit and thrill over the thigh had disappeared. The liver no longer was palpable. The spleen was greatly reduced in size but still could be palpated one finger's breadth below the costal margin. Four days later, the spleen no longer was palpable.

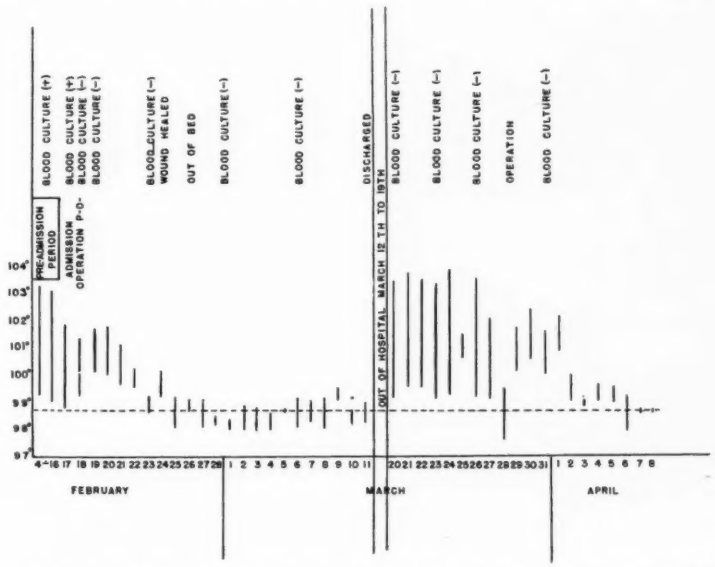

Fig. 4. Graphic chart indicating temperature and blood cultures in relationship to operations.

The first blood culture, taken 4 hours after operation, was reported sterile after 14 days of incubation. Four additional blood cultures were taken, on the 1st, 5th, 10th, and 16th postoperative days, respectively (Fig. 4). These likewise were reported sterile after 14 days of incubation. No chemotherapy was administered during the postoperative course and, accordingly, the prompt disappearance of organisms from the blood stream could be ascribed only to the operative procedure. The patient was kept in the hospital for 21 days following operation, in order to observe him closely and to repeat various investigative studies (Tables I, II, III). At the time of discharge, the temperature had been essentially normal for 2 weeks; and he was gaining weight and appeared to be in excellent general physical condition.

Subsequent course. Three days after returning home, the patient experienced a sensation of fulness and pressure in the abdomen. The following day, severe diarrhoea developed and the temperature rose to 100.4 degrees F. During the next 5 days irregular fever, ranging as high as 103.6 degrees F., and nightly sweats were present. Accordingly, he was advised to re-enter the hospital for investigation.

On admission March 20, 1941, to the medical service of Dr. George Baehr, temperature was 101.4 degrees F., pulse 92, and respirations 20. He did not appear acutely ill and his general condition seemed even better than when last observed. The cardiac findings were unchanged except for the presence of a short, faint, high-pitched, apical systolic murmur which presumably was of functional origin. The blood pressure in the extremities was essentially the same as at the time of discharge 9 days previously. The liver was not palpable. The spleen however, again was *palpable* 3 fingerbreadths below the costal margin. The operative wound was well healed, and all clinical evidence of the previously existing arteriovenous aneurysm was absent.

X-ray examination of the chest disclosed further diminution in the size of the heart and previously prominent pulmonary vessels. The electrocardiogram revealed no change as compared with the tracing made shortly before discharge from the hospital. The phonocardiogram revealed a faint systolic murmur over the precordium; a tracing made over the region of the femoral vessels on the left side failed to reveal the presence of abnormal sounds. The specific gravity of the urine was 1026. Albumin and dextrose were absent. The microscopic examination was negative. The hemoglobin content of the blood was 70 per cent. There were 4,600 leucocytes per cubic millimeter, of which 44 per cent were segmented polymorphonuclear leucocytes, 29 per cent nonsegmented polymorphonuclear leucocytes, 19 per cent lymphocytes, 5 per cent monocytes, and 3 per cent eosinophiles. A blood smear did not reveal macrophages. The erythrocyte sedimentation rate was normal. Culture of the stool revealed only enterococci and Bacillus coli.

Three blood cultures, performed during an 8 day period of observation, were negative after 14 days of incubation. Blood agglutination tests for heterophile anti-body, dysentery, typhoid, paratyphoid, Bacillus abortus, and Bacillus melitensis also were negative. During this period, the temperature ranged between

TABLE I.—STUDIES OF THE CIRCULATION

	Before operation		After operation	
Character of pulse	Corrigan		Normal	
Left common femoral artery Size Pulsation	Large Marked		Smaller Normal	
Right Arm	B. P.	Pulse	B. P.	Pulse
Basal	132/70	112	112/64	92
Compression of left common femoral artery	138/80	92	112/64	92
Left arm				
Basal	124/60	108	108/66	92
Compression of left common femoral artery	132/74	96	108/66	92
Right thigh	160/70	110	120/68	92
Left thigh	180/ 0	110	130/80	92
Oscillometrics	Right	Left	Right	Left
Thigh	3¾	20	9	9½
Calf	2½	4¼	7	7
Ankle	1¾	1½	4½	3½

TABLE II.—STUDIES OF THE CIRCULATION

	Before operation	After operation
Venous pressure Right upper quadrant pressure	7.5 cm. No rise	8.5 cm. No rise
Saccharine time	15 sec. (febrile)	11 sec. (afebrile)
Cardiac output		
Basal	7.2 L/min.	5.5 L/min.
Compression of common femoral artery	5.5 L/min.	5.5 L/min.
2 minutes after release	6.8 L/min.	. . .
Cardiac murmurs (auscultation)		
Apex	Soft systolic	None
Pulmonic area	Harsh systolic and diastolic	None
Bruit		
At site of aneurysm	Loud to-and-fro	None
Over great vessels	Present	None
Pulsation, retinal artery	Present	Absent

99.2 and 103.8 degrees F. and the pulse rate between 82 and 120. In spite of the irregular fever, the patient continued to look quite well, and various circulatory studies confirmed the absence of the previously existing arteriovenous communication.

In view of the pre-existing infection, it appeared essential to exclude a recurrence of sepsis as the cause of the symptoms. It was postulated that if sepsis were present, it most likely was derived either from a previously unrecognized endocarditis or from a thrombophlebitis involving vascular channels immediately adjacent to the former site of the arteriovenous aneurysm. However, the diagnosis of recurrent subacute Streptococcus viridans septicemia appeared to be excluded by the negative blood cultures. (In an effort to exclude the diagnosis of thrombophlebitis involving vascular channels in the thigh, one of the blood cultures was taken directly from the left common femoral vein.) Furthermore, the erythrocyte sedimentation rate now was normal and leucopenia was present. Finally, the re-enlargement of the spleen seemed too marked and too rapid to be consistent with the diagnosis of subacute bacterial septicemia. The history of abdominal pain and diarrhoea at onset, together with the acute enlargement of the spleen and leucopenia, suggested the possibility of an intercurrent typhoid or paratyphoid infection. However, these diagnoses were excluded by appropriate examinations of the stool and blood. Finally, in view of the fact that the patient had received a number of transfusions during the first admission, the diagnosis of accidental malarial infection was entertained. The rapid splenic enlargement and leucopenia appeared to be consistent with such a diagnosis but several blood smears proved negative for plasmodia. After consultation with Dr. Harold Neuhof, it was decided as a precautionary measure to re-explore the original operative site for evidence of local thrombophlebitis. In spite of the fact that the blood cultures were sterile, it was considered possible that such a focus might be found. Furthermore, it was the consensus that even if exploration proved negative, no harm would result.

TABLE III.—ELECTROCARDIOGRAPHIC STUDIES

Compression of Left Common Femoral Artery

	Before operation	After operation
Pulse rate Before compression After compression	105/min. 90/min.	76/min. 76/min.
Axis deviation	Right	Right
T wave: lead III Before compression After compression	Inverted Upright	Upright Upright
RT: lead III Before compression After compression	Slight depression Isoelectric	Isoelectric Isoelectric

On March 28, 1941, an operation was performed (by A.S.W.T.), under ethylene anesthesia. The incision was begun at a point above Poupart's ligament and carried downward, mesial to the old operative scar, to the junction of the upper and middle thirds of the thigh. The common femoral artery and vein were exposed and found to be of approximately *normal* caliber. (The artery measured approximately ½ inch and the vein ⅜ inch, in diameter.) The common femoral and superficial femoral arteries were freed and retracted laterally in order to expose the point of confluence of the superficial femoral vein and the short, proximal stump of the previously excised deep femoral vein. No abnormality was to be noted in or about these structures. The common femoral vein was divided between ligatures, at the level of Poupart's ligament. The vein then was freed in a downward direction and the stump of the deep femoral vein, together with a 4 inch section of the superficial femoral vein, was excised. Oozing, from the surrounding tissues, was

controlled by a small gauze packing which was left *in situ* and brought out through the lower angle of the wound. The fascia was sutured loosely and the skin was closed with clips.

The pathological report upon the excised specimen was as follows: "Vein showing focal phlebosclerosis, otherwise no significant change is present."

The immediate postoperative reaction was satisfactory. During the first 3½ days, the temperature ranged between 100 and 102.4 degrees F. A blood culture, taken on the third postoperative day, was reported sterile. Four grams of sulfapyridine was administered on the day of operation and 6 grams on the first postoperative day. The temperature became normal on the 5th day after operation.

The wound healed kindly, the drain and the skin clips being removed on the 5th postoperative day. By the 7th postoperative day, the spleen had diminished appreciably in size. The patient was discharged on the 11th postoperative day in good physical condition. At the time of discharge there was moderate edema of the left lower extremity.

When last observed in the follow-up clinic on March 17, 1942, the patient had gained 42 pounds in weight and was entirely free of symptoms. The operative incisions were well healed; and edema of the left lower extremity, noted after the second operation, no longer was present. The spleen was not palpable. The heart was essentially normal in size. The blood pressure was 122/74. The electrocardiogram was normal. The cardiac output was normal (4.6 liters). The phonocardiogram revealed a very faint systolic murmur over the precordium which was interpreted as being of functional origin. A sound tracing taken from the thigh failed to disclose any abnormality. On the basis of the complete absence of symptoms and with the findings herein noted, recovery from both the arteriovenous aneurysm and subacute Streptococcus viridans bacteriemia was considered to have taken place.

Fig. 5. Roentgenogram of chest 6 months after excision of arteriovenous aneurysm. Note reduction in size of heart.

SUMMARY

The patient, a male aged 26, suffered a through-and-through gunshot wound of the left thigh 9 years previously. Within a year of the injury, evidence of an arteriovenous aneurysm associated with manifestations of cardiac insufficiency developed. Although the diagnosis of a "heart condition" was made, the existence of an arteriovenous aneurysm was not recognized. Following the extraction of a tooth and some dental reparative work, 7 years after the original injury, symptoms of sepsis began. The manifestations continued for almost 2 years before the diagnosis of arteriovenous aneurysm and subacute Streptococcus viridans septicemia was made. Clinical and laboratory investigations failed to reveal conclusive evidence of an infective endocardial lesion as the source of the sepsis. It therefore was postulated that the focus of infection was situated within the arteriovenous aneurysm. Under the circumstances, surgical excision of the aneurysm appeared to offer a hope of cure. At operation, a large arteriovenous aneurysm involving the profunda femoris artery and vein, and filled with vegetations containing Streptococcus viridans, was found and excised widely. The course following operation was one of rapid improvement, the local and constitutional manifestations of arteriovenous aneurysm disappearing rapidly and the blood cultures becoming sterile promptly. In view of the fact that chemotherapy had been administered prior to operation for one year without effect and was not administered at all after operation, the sharp termination of the sepsis appeared attributable solely to the operative removal of the infected aneurysm. The patient was discharged from the hospital 3 weeks after operation in excellent physical condition, all postoperative blood cultures having been reported sterile.

He was readmitted 9 days later because of abdominal pain, diarrhoea, recrudescence of septic temperature, and enlargement of the

spleen. During an 8 day period of observation 3 blood cultures, including one taken directly from the left common femoral vein, were reported to be sterile. After a number of infectious diseases including typhoid fever and malaria has been excluded, it was decided to re-explore the old operative site for evidence of thrombophlebitis despite the negative blood cultures.

At operation, no abnormality was found locally; but the common femoral vein, the upper portion of the superficial femoral vein, and the stump of the deep femoral vein were excised as a precautionary measure. Microscopic examination of the specimen failed to reveal the presence of any significant changes. Following operation, recovery ensued rapidly.

One year has elapsed since the last operation and the patient remains entirely well. This is the second case of acquired arteriovenous aneurysm, complicated by subacute Streptococcus viridans septicemia, in which recovery has followed surgical treatment.

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CONTRAST MEDIA IN CYSTS AND ABSCESSES OF THE CEREBRAL HEMISPHERE

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THE effectiveness and ease of performance of any technical procedure is enhanced by its simplification. Thus in surgery, that approach to a large, deep seated lesion which is most direct is the one of choice, provided vital structures are not traversed.

It has been the experience of all neurosurgeons in attempting ventricular air injection or biopsy of a cerebral tumor, to enter unexpectedly a cystic cavity with the exploring needle, xanthochromic fluid or pus being obtained. To approach such a lesion in the most direct manner and thus simplify operative procedure, the use of a contrast medium is desirable.

Air and iodized poppy seed oil have been used for this purpose but do not mix with fluid contents. Sodium iodide is miscible and Rockey instilled a 20 per cent aqueous solution into a brain abscess to show "the postoperative course after the original drainage had been instituted." The visualization in this case was excellent. It showed, moreover, how a portion of the collapsed abscess capsule had wrapped itself around the drainage tube and caused loculation of the abscess cavity rather than the desired evacuation. Colloidal thorium dioxide (thorotrast) is less irritating than sodium iodide, mixes readily, and has the added advantage of being phagocytized by the cellular elements of an abscess wall, making the capsule radio-opaque. This has been previously demonstrated by me. Jessen first reported the use of colloidal thorium dioxide for ventriculography. In a discussion on this same subject, Freeman and Schoenfield suggested that this contrast medium be used in cysts or encapsulated abscesses of the brain.

The following histories are selected from a small group of cases in an effort to show the value of colloidal thorium dioxide cystography:

From the Department of Surgery, The University of Michigan Clinic of Dr. Max M. Peet.

CASE 1. A. L., a 14 year old girl, entered the University Hospital with a 6 months' history of gradually increasing intracranial pressure. There was found on examination marked papilledema and a quadrantic type of homonymous hemianopsia but little else in the way of localization.

A ventriculogram was performed which gave evidence of a large expanding lesion of the left cerebral hemisphere. A trephine opening was then made on the left, a half inch above and behind the ear. A cyst was entered with the exploring needle close to the surface of the brain. Twenty cubic centimeters of somewhat viscous xanthochromic fluid was removed and 5 cubic centimeters of colloidal thorium dioxide (thorotrast) was injected.

Roentgen-ray studies revealed a large cyst. A lateral film, taken with the forehead up allowing gravity to aid in filling out the posterior wall of the cavity, revealed a perfectly smooth contour. A lateral film with the forehead down, however, outlined a mural nodule attached to the anterior wall (Fig. 1).

Under avertin anesthesia, the trephine incision of the left side was carried forward and superiorly in the shape of a hockey stick. The temporal muscle was stripped downward, thus exposing the squama of the temporal bone. Trephine openings were made to center a small bone flap directly over the mural nodule. These were connected with the Gigli saw, and the bone was removed to be replaced as a free graft. The dura was opened. The underlying brain substance was extremely thin and an opening was made into the cyst. The mural nodule which was about the size of an English walnut was seen anteriorly exactly as pictured in the x-ray film. It was widely excised with the electrosurgical unit.

Convalescence was uneventful and the patient was discharged on the tenth postoperative day. She has remained well for the past 2 years. There has been no change in the hemianopic defect except for some concentric contraction which was attributed to secondary optic atrophy. The tumor was shown microscopically to be a fibrillary astrocytoma.

This lesion, as the ventriculogram suggested, was of considerable size. Judging from the air studies alone, to have exposed it completely would have meant turning down a large bone flap. Cushing long ago showed that if the mural nodule of an astrocytoma were removed the cyst wall need not be dealt with. By accurately visualizing the mural

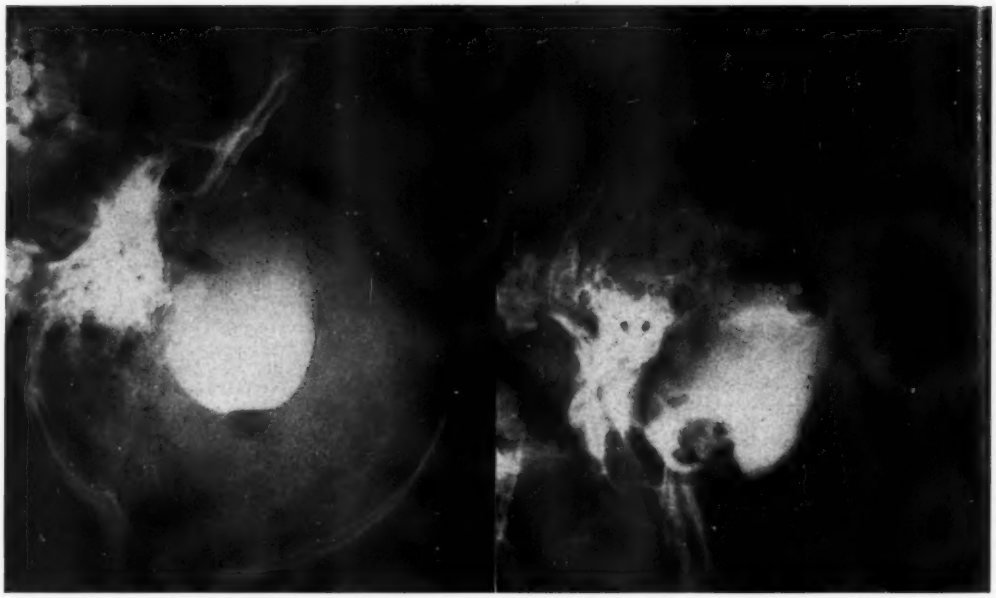

Fig. 1. Case 1. a, left, Lateral roentgenogram with forehead up showing smooth posterior wall outlined by 5 cubic centimeters of colloidal thorium dioxide which has thoroughly mixed with the fluid contents of the cyst. b, Lateral projection with forehead down outlining the mural nodule anteriorly.

nodule in this case an effective operation was carried out by means of a comparatively simple procedure. It is doubtful if 50 cubic centimeters of air could have demonstrated this lesion as well as 5 cubic centimeters of colloidal thorium dioxide.

CASE 2. J. G., a 62 year old man, was admitted to the hospital because of difficulty in speaking and headache, both of which had been present for 3 months.

On examination, the visual fields revealed a suggestive right homonymous hemianopsia but no papilledema. There was a slight right sided hemiparesis. The patient had a mixed expressive receptive type of aphasia. No definite right sided sensory changes could be elicited but the patient was unable to co-operate fully. A diagnosis was made of a lesion of the left temporoparietal region, probably tumor.

A trephine opening was made on the left, an inch above and half an inch behind the top of the ear (this is somewhat higher than the usual opening made in this clinic for ventricular air injection). When the dura was opened, the cortex appeared normal. At a depth of about 3 centimeters a cyst was entered with the exploring needle though there was no abnormal sense of resistance. About 15 cubic centimeters of viscid yellow fluid was obtained and 5 cubic centimeters of colloidal thorium dioxide instilled. X-ray studies were completed after closure of the wound and demonstrated a deep seated cavity with an irregular, ragged wall (Fig. 2).

The patient was returned to the operating room where a biopsy specimen was taken with the hollow needle. The microscopic diagnosis was glioblastoma multiforme. The patient was discharged as hopeless on the fifth postoperative day.

The glioblastoma multiforme, because of its microscopic infiltrative growth, defies surgical removal. Though biological or physicochemical methods of treatment may be developed in the future, the fact remains that this lesion does not respond to gross surgical excision, roentgen-ray therapy or both. The first real contribution to the palliation of this lesion was the "internal decompression" of McKenzie. Spurling, on the other hand, when a glioblastoma multiforme is strongly suspected, takes a biopsy specimen and does not ordinarily operate if the microscopic examination brings confirmation.

Cyst formation is common in the glioblastoma multiforme and is undoubtedly due to central necrosis within the tumor itself.

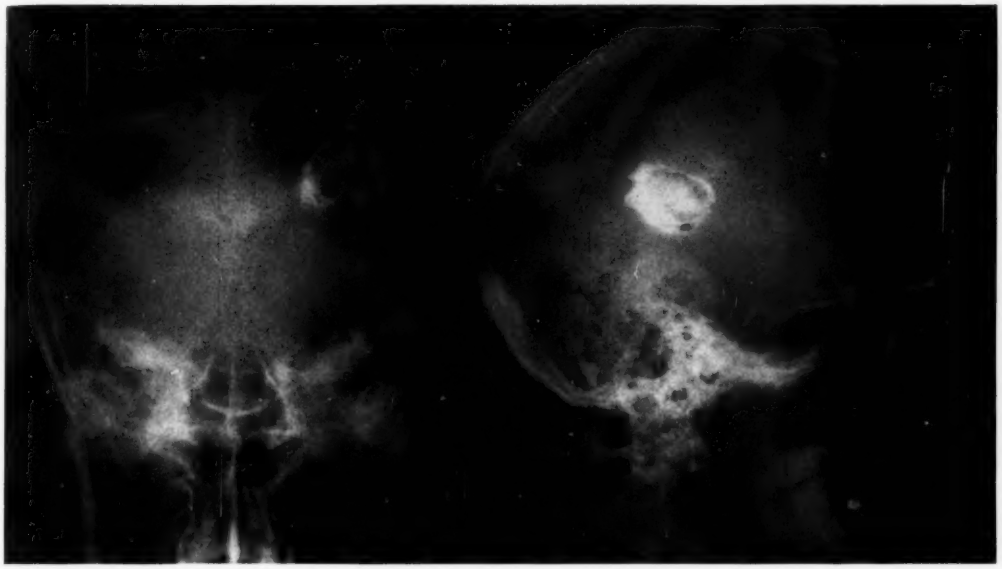

Fig. 2. Case 2. Ragged irregular outline of the cyst of a glioblastoma multiforme.

Consequently, the cyst is always surrounded by solid or semisolid necrotic tumor and the wall is poorly defined. On surgical incision into such a cavity it tends to obliterate due to the rapid expansion on all sides of the broken down, edematous, discolored tumor tissue. One might draw a comparison between this lesion and the unencapsulated abscess of the brain secondary to pulmonary suppuration (Fig. 3). Both form their cavities by a process of liquefaction necrosis without any tendency toward walling off. There is consequently a certain resemblance as shown by contrast media.

From the above discussion I have reached the following conclusion: If on attempting biopsy or ventriculogram, a cyst is entered it should be outlined by the injection of colloidal thorium dioxide. If a ragged, irregular cavity is demonstrated one may be fairly certain of the diagnosis of glioblastoma multiforme or at least, of a malignant glioma. The tumor must, of course, be subjected to biopsy examination for confirmation and in this procedure, again, the contrast medium is of value in showing where best to take the specimen. Microscopic diagnosis from biopsy material is admittedly not infallible, but the presence of a malignant type of growth can usually be determined. Every case is a law unto itself but if the rolandic area or the various speech centers are involved, operation is inadvisable.

Case 3. H. O., a 57 year old male, was admitted to the Hospital in a stuporous condition. He could be roused enough to demonstrate a left sided hemiplegia which seemed complete. There was a previous 6 months' history which was undoubtedly related to a cerebral lesion.

On attempting ventricular oxygen injection through a trephine opening, a half inch above and behind the right ear as is the usual procedure in this clinic, a cyst was entered and dark xanthochromic fluid was obtained. Between 6 and 8 cubic centimeters of colloidal thorium dioxide were introduced. X-ray studies gave evidence of a temporoparietal cyst with a large mural nodule (Fig. 4).

The patient was returned to the operating room and under local anesthesia, a moderate sized bone flap was turned down directly over the lesion. The cyst was entered after traversing a little less than a centimeter of brain substance. At the posterior medial aspect of the cyst wall an irregular brownish mural nodule about the size of a large plum was found. This was completely excised together with the cyst wall until normal white substance was everywhere encountered, the tumor having been thought to be a cystic oligodendroglioma. (Cushing and Eisenhardt have shown that this type of tumor

Fig. 3. Outline typical of unencapsulated abscess metastatic from pulmonary suppuration.

tends to recur rapidly.) During this process it was found that tumor substance extended posteriorly almost to the occipital pole, basally to the inferior surface of the temporal lobe and anteriorly to the midparietal area. The compressed right lateral ventricle was entered and the choroid plexus clipped. The upper surface of the tentorium was widely exposed and to some extent, the right side of the falx.

The patient made an excellent convalescence except for a complete left homonymous hemianopsia with splitting of the macula. The tumor was histologically thought to be a primary sarcoma of the brain.

The patient returned 8 months later in a semicomatous condition. Operation was again performed and an enormous recurrence was found. Again the tumor seemed to be completely excised. Immediate convalescence from the second procedure was surprisingly good but he returned 3 months later and died. The autopsy, which was limited to the head, revealed a massive recurrence.

This tumor from the point of view of cystography with colloidal thorium dioxide, might be considered as midway between a benign lesion and a malignant one. The fact that the cyst was extremely large suggested the former while the size of the mural nodule and the slight irregularity of the cyst wall was in favor of the latter. Where there is real doubt as to operability, direct attack upon the lesion itself rather than biopsy is indicated.

The following case is reported in detail, first as a method of handling an acute subdural abscess, and second because a contrast medium was of such help in dealing with a complicating cerebral abscess.

CASE 4. A 17 year old boy entered the University Hospital with the following history. Two weeks previous to admission the patient had suffered an ordinary head cold. This began to subside within a few days but bilateral frontal headache persisted. One week before admission the headache became more severe on the right and swelling of the right upper eyelid developed rapidly. Two days later, the swelling had reached a peak and rapidly subsided. There was now noted, besides increasing headache, stiffness of the neck and increasing irritability. Two days before admission, nausea and projectile vomiting developed and numbness of the left hand was complained of. This was rapidly followed by weakness of the entire left side.

Examination revealed an extremely ill and apathetic patient. The temperature was 103 degrees, the pulse 78, and respiration 20. There was stiffness of the neck and a positive Kernig's sign. Fundoscopic examination revealed early papilledema. There was a left central type of facial paralysis and the tongue deviated to the left, on protrusion. There was marked weakness of the left arm and slight weak-

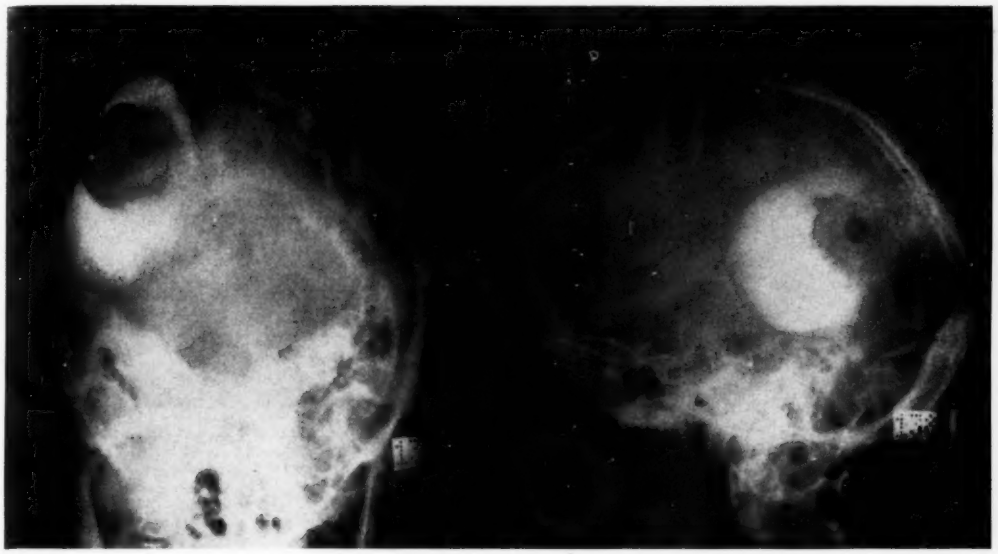

Fig. 4. Case 3. Cystogram of tumor diagnosed as primary sarcoma of brain.

ness of the left leg. Babinski's sign was negative bilaterally. There was a leucocytosis of 20,000. A pansinusitis on clinical examination was confirmed by x-ray studies.

A diagnosis of subdural abscess was made. Inasmuch as the infection was thought to have extended through the right frontal sinus, epidural pus was also suspected. It was decided first to perform a right sided Killian operation.

At operation by Dr. James Maxwell of the department of otology, an empyema of the right frontal sinus was found. The entire wall of the frontal sinus was removed but there was no evidence of erosion of the inner table. The ethmoidal cells were found to be grossly infected and were exenterated. The anterior face of the sphenoid was removed and the sphenoid found to contain thick pus. The inner table of the frontal sinus was removed but there was, in this case, no evidence of epidural pus or even granulation tissue over the tense dura. It was thought best to expose the dura through a clean field above the operative site. It was believed that the patient's condition warranted waiting until the following day before this procedure was carried out.

The patient was carefully watched for the next 24 hours since any further evidence of acute increase in intracranial pressure would have necessitated immediate operation.

At the end of this period the patient's condition was unchanged. Under local anesthesia, a trephine opening was made over approximately the center of the frontal bone. The dura appeared tense and whiter than normal. When the dura was opened there was an escape of a large amount of thick greenish white, odorless pus which was extra-arachnoid. The incision was now enlarged and an area of bone about the size of a silver dollar was removed with the rongeur. The dura was further opened in a stellate manner, the pus extending in all directions. There now developed a herniation of the brain through the defect, making retraction of the brain impossible. In order to gain relaxation so that all pus could be removed and adequate drainage be established without making a tremendous bone defect, it was decided to perform a lumbar puncture.

The patient was turned and the lumbar puncture needle was introduced. The pressure was between 600 and 700 millimeters of water. The fluid was cloudy and contained 5,600 cells per cubic millimeter. After approximately 50 cubic centimeters had been obtained, the brain commenced to pulsate and to drop away from the dura. With the lumbar puncture needle left in place, the surface of the brain was now easily depressed with a lighted retractor, the entire surface of the brain being explored back to at least the midparietal region. All pus was removed by suction even as far forward as the tip of the frontal pole. The wound was washed out with Ringer's solution and hydrogen peroxide, inasmuch as it was thought that the pus could not be extended any farther than it had already gone. Rubber tissue drains were inserted as far as possible in four directions; to the postparietal region, the midline, the tip of the frontal pole, and down onto the temporal lobe near its tip. This procedure was carried out without difficulty and with almost no trauma to the arachnoid since the hemisphere following lumbar puncture retracted from the dura for

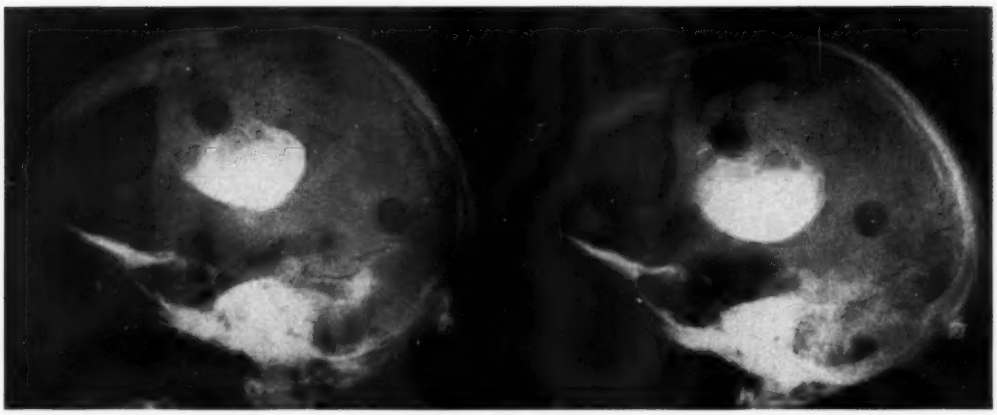

Fig. 5. Case 4. a, left, Encapsulated abscess of brain secondary to subdural abscess. The large anterior skull defect was made for drainage of the subdural abscess; the trephine opening just posterior was used for the injection of the colloidal thorium dioxide. Posteriormost trephine is that used for ventricular oxygen injection. b, Four days later showing increase in size of the abscess which has taken place.

at least 1.5 centimeters in all directions. The drains were gradually removed within the course of the next 4 days. Convalescence was comparatively uneventful, the mild herniation noted at times was controlled by lumbar puncture until granulation was complete.

Three weeks after discharge the patient returned to the hospital with an increasing left hemiparesis having had one generalized convulsion. There was a moderate bulging of the decompression.

A trephine opening was made just posterior to the frontal defect in order to reinspect the subdural space. When the dura was opened a normal convolution was seen showing that the subdural abscess had been apparently cured. The wound was closed.

A needle was now inserted through the scalp over the large frontal defect and was passed deeply in several directions. No abscess was encountered.

An encephalogram was made a few days later by the lumbar route which showed displacement of the left lateral ventricle to the left but did not accurately localize the abscess. A few days later a ventriculogram was made through a left sided trephine opening. This gave definite evidence of a large lesion of the right parietal region.

The trephine opening which had been made posterior to the frontal defect previously, in order to inspect the subdural space, was reopened. A needle was passed downward through the brain substance and at a depth of about 3 centimeters, met with an elastic resistance through which the needle was plunged. About 60 cubic centimeters of pus was obtained (Fig. 5) and 8 cubic centimeters of colloidal thorium dioxide instilled. X-ray studies (Fig. 5) revealed a large abscess cavity. Six days later the abscess cavity was seen to have increased in size by x-ray. The heavily encapsulated abscess was uncapped and drained. Recovery was uneventful.

A year later an encephalogram was performed because of a few Jacksonian seizures. This showed slight dilatation of the entire ventricular system but no evidence of any recurrence.

At the present time this patient feels perfectly well and goes swimming daily.

Here we have the problem of a patient with a large bulging frontal decompression and a suspected subcortical cerebral abscess which might have been anywhere in that cerebral hemisphere. The abscess was finally entered with the exploring needle and outlined with colloidal thorium dioxide. Its exact position and the point at which it lay closest to the surface was determined.

Another case might be briefly mentioned in this connection. A 45 year old doctor entered the hospital in coma with a 3 weeks' previous history of otitis media. An encapsulated abscess was tapped through an incision just above and in front of the right ear (Fig. 6). Colloidal thorium was instilled and a small decompression made over where the abscess was thought to be most superficial. Roentgenograms were not taken at this time because of the patient's precarious condition. Subsequent x-ray films showed that this opening had been placed higher than it would have been had films been obtained before decompressing. In spite of this, the abscess migrated toward the surface sufficiently within 3 days so that uncapping and drainage were per-

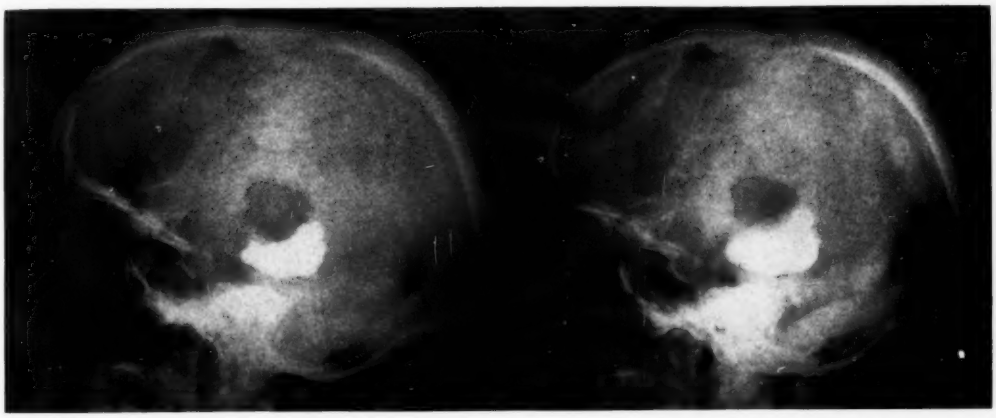

Fig. 6. a, left, Decompression was placed too high because the abscess was not visualized previously. b, Three days later, the capsule is shown to have risen toward the decompression.

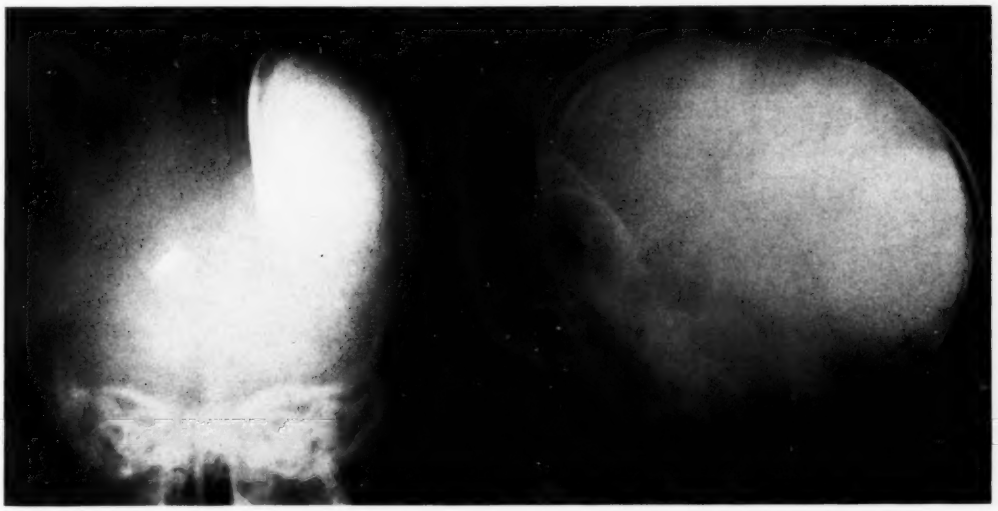

Fig. 7. Case 5. Colloidal thorium dioxide thoroughly mixed with pus in infected subdural hematoma.

formed at that time without difficulty. The most recent x-ray films which were taken 3 months after operation show stereoscopically a fine circular line less than 1 centimeter in diameter in the substance of the brain just above the tegmen tympanum. This is undoubtedly due to colloidal thorium dioxide in what remains of the capsule. It is probably of no significance as the patient is back at full time work, but it will be followed with interest.

CASE 5. R. F., a 7 months old male infant, was admitted to the hospital with the appearance of being *in extremis*. The child according to the parents' story, had been well up to the age of 4 months at which time he had developed bilateral otitis media and a pneumonia which was confirmed by x-ray. This had gradually cleared but a spastic tetraplegia with enlargement of the head had developed.

On examination the infant was found to weigh but 10 pounds. Though the head was generally enlarged this was most marked on the left side. There was no papilledema. The leucocyte count was

15,800 and the temperature was 99 degrees. A diagnosis was made of abscess of the left cerebral hemisphere, metastatic from the lung rather than secondary to the otitis media, which in my experience so rarely causes abscess in infants.

A needle was passed through the left side of the anterior fontanelle to a depth of about 3 centimeters. On withdrawing the stylette 45 cubic centimeters of pus was obtained, following which, 15 cubic centimeters of colloidal thorium dioxide was injected (Fig. 7).

X-ray studies, to our great surprise, revealed the contrast medium to be in the left subdural space. By means of two large trephine openings, one in the frontal and one in the parietal region, the subdural space was entered. There was a purulent membrane attached to the inner surface of the dura. There was a heavy inner membrane apparently holding the brain down. Several incisions were made into the latter but it was soon obvious that removal of much of this membrane was out of the question. Specimens of both membranes were taken for pathological examination. Multiple rubber tissue drains were placed in the subdural space.

The infant now made an amazing improvement. The drains were removed on the sixth postoperative day. He was discharged with the incisions completely healed, 7 weeks later.

Pathological examination of the membranes revealed that infection had developed in what had undoubtedly been a chronic subdural hematoma. Culture of the pus obtained at operation showed Staphylococcus aureus.

On examination five months later, the child could still not sit up alone but noticed things and was making an effort to use both upper extremities. It has been impossible to contact the family since that time.

The advantage of using a contrast medium which mixed freely with the contents of a purulent cavity is obvious in this case. The operator had thought that he was dealing with an intracerebral abscess until the x-ray studies were obtained.

CONCLUSIONS

1. Colloidal thorium dioxide can be used to advantage in outlining cystic tumors of the cerebral hemispheres. This not only gives a clue to the pathological nature of the neoplasm but simplifies the surgical approach should operation be deemed advisable.

2. This contrast medium is of value in the treatment of the encapsulated abscess of the brain whether it be dealt with by repeated tapping after the method of Dandy, open drainage, or complete excision as performed by Vincent.

3. Colloidal thorium dioxide has the advantage over iodized poppy seed oil or air in that it mixes readily with fluid contents and may be phagocytized by the surrounding wall of an abscess so that the capsule itself will be visible in the roentgen-ray within 3 days or less.

4. There can be little danger in the use of colloidal thorium dioxide from the effect of long standing radioactivity since the main mass of this substance is removed in the evacuation of the cavity.

5. It is suggested that there might be wider application in the field of general surgery as in visualization of an empyema cavity. In the drainage of a thoracic empyema, the difficulty increases as the cavity becomes smaller. It is, at this later stage, that the colloidal thorium dioxide which has been phagocytized by the empyema wall might show when obliteration is complete.

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SO CALLED LATERAL ABERRANT THYROID TUMORS

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THE existence in the lateral regions of the neck of cellular masses derived from thyroid tissue has been recognized for more than a hundred years (15), but no serious attempt was made to describe these masses as a separate clinical entity until late in the nineteenth century when isolated reports of cases began to appear in the English and the German literature (1-6).

By 1900, enough cases of these tumors had been reported to give rise to speculation concerning the origin and the pathological characteristics of the growths. There was evidence to indicate that the thyroid gland originated from two separate anlagen, an unpaired median component and paired lateral components, which fused early in fetal life. The earliest school of thought, and by far the largest one today, attempted to explain the origin of "lateral aberrant thyroids" by some abnormality in the development of the lateral anlagen. Schrager, in 1906, expressed the belief that these masses were essentially benign tumors arising as a hyperplasia of normal thyroid elements detached from the lateral anlagen before fusion, in response to an increased demand for thyroxin created by subefficient function of the thyroid proper.

The predominantly papillary nature of these tumors and their frequent association with similar tumors in the corresponding thyroid lobe were first pointed out by Low in 1903. He emphasized that their rate of growth was slow and that metastasis to distant regions was rare, spread tending to occur rather by local invasion of the lymph channels. Many years later Billings and Paul reiterated these observations. The peculiar structure of these tumors led to the belief that "lateral aberrant thyroids" were derived not from normal thyroid elements but from tissue which was constitutionally inferior to that of the thyroid proper.

Kingsbury demonstrated that the lateral anlagen degenerated after fusion with the median anlage and probably disappeared completely. Leech, Smith, and Clute and, later, Cattell expressed the belief that "lateral aberrant thyroids" originated from fetal rests derived from the degenerated lateral anlagen and were intrinsically malignant. They concluded that the frequently coexistent papillary tumor in the corresponding thyroid lobe arose from a fetal rest derived from the same source. Crile (7, 8) concurred in their explanation of the origin of thyroid and "aberrant" tumors, but expressed the opinion that these tumors were remarkably benign in their behavior.

In 1931 Dunhill revived Schrager's conception of the physiological stimulus concerned in the genesis of "lateral aberrant thyroids." He expressed the belief that the lateral anlagen were constitutionally inferior to the median anlage and that tissue derived from them, whether situated within or without the thyroid lobe, was prone to undergo papillary change in response to stimulation by ordinary physiological demands. Thus arose the theory of "activated rests." Van den Wildenberg expressed the belief that the papillary cystadenomas so formed were precancerous and that further stimulation by relative thyroid insufficiency caused them to become malignant.

Greteman and Russum extended this idea to account for recurrences, stating that continuation of the stimulus caused other tiny and previously unaffected rests, missed at the first operation, to develop into palpable tumors. They suggested that the thyroid itself be explored because it frequently is involved by a similar tumor.

In 1940 Ward further elaborated the theory of "activated rests." He, like Dunhill, expressed the belief that stimulation of any tissue derived from the lateral anlagen resulted in papillary change; however, he was of the opinion that this change, occurring among children, was in a reversible stage and would regress if the stimulus were removed by treatment of the patients with iodine, whereas, among adults, owing to the loss of some cancer-resisting factor, the process became irreversible and went on to malignancy. Thus he advocated radical surgical procedure and radiation in the treatment of adults. Cohn and Stewart, in the same year, stated the belief that the location of a papillary tumor within or without the lateral thyroid lobe depended on whether embryonic tumor cells were split off the lateral component before or after fusion took place. If this splitting off occurred both before and after fusion, coexistent primary tumors appeared in the thyroid and side of neck. They stressed importance of complete excision of tumor to prevent recurrence.

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A second school of thought, much in the minority, held that "lateral aberrant thyroids" were metastatic carcinomas in the cervical lymph nodes secondary to primary carcinoma of the corresponding thyroid lobe. Wohl, in 1917, advised thinking of this possibility when a so called lateral aberrant thyroid was found and Eberts, in 1933, advocated removal of the corresponding thyroid lobe even though it appeared normal. It was pointed out by one of us (J. deJ. P.) in 1934 (25) and again in 1939 (26) that these lateral masses, incorrectly termed "lateral aberrant thyroids," were in reality, true metastatic carcinomas.

A few other investigators explained the origin of these tumors as nests of normal thyroid cells which either occupied their aberrant position because of natural distribution (31, 35) or were dragged away from the thyroid proper by muscles, vessels, and nerves which were developing (9, 23, 37).

George Crile, Jr., in two recent papers, swung back to the opinion held by Schrager that these were benign tumors. Crile stated that papillary tumors of the thyroid gland, in his experience, did not metastasize to lymph nodes and that "lateral aberrant thyroids" were not metastatic carcinomas and were not as a rule malignant. He expressed the opinion that the finding of a hard, palpable tumor in the thyroid gland, together with multiple nodules in the neck, was confirmatory evidence of the presence of "lateral aberrant thyroid tumor." He expressed the belief that because these tumors were benign and did not spread, because they did not recur after operation for their removal, and because they never caused the death of the patient, complete cure would result, provided they were removed completely.

Since 1920 the microscopic diagnosis of malignant disease in thyroid tissue has received much attention. Graham (12, 13) stated the belief that vascular invasion was the main criterion in the diagnosis of the nonpapillary type of cancer; that capsular invasion and lymphatic invasion were the criteria in the purely papillary types. Ward and others (22, 23) stated that capsular invasion and lymphatic and vascular invasion were the only reliable signs of malignant change. Neither Ward nor Crile believed that the presence of lymphoid tissue in an "aberrant thyroid" was a sign that the tumor was a metastatic lesion in a lymph node. However, Broders (3, 4) expressed the opinion that the most reliable signs of malignancy were cellular undifferentiation and mitosis.

ANALYSIS OF FIFTY-FOUR CASES

In the selection of cases at the clinic to correspond with those described by other writers, all those were chosen first in which a benign or a malignant tumor of thyroid tissue was discovered in the lateral region of the neck, without any gross connection with the thyroid gland itself. This group included cases in which the lateral cervical tumor had been removed elsewhere prior to the patient's visit to the clinic and other cases in which it had been removed or in which biopsy had been made at some time after operation on the thyroid gland. In many cases there had been also a tumor in the thyroid itself before, at the time of, or after, operation on the cervical tumor. The whole group was divided into two series: the first series, 54 cases, included only cases in which the lateral cervical tumor was the patient's main complaint or was the main reason for performing the operation. In these cases the cervical tumors were considered "lateral aberrant thyroids" irrespective of the presence of a thyroid tumor. In all the other cases there were malignant tumors of the thyroid gland which were themselves the reason for operating, and the associated lateral cervical tumors were unquestionably, in our opinion, regional metastatic lesions. In 15 cases of the second series, the cancers were papillary; microscopic analysis of these cancers was made for comparison with the tumors in the first series of cases.

Of the 54 patients in the first series, 29 were females and 25 were males. The highest age incidence occurred in the fourth decade among the former, in the third decade among the latter. The clinical diagnosis most commonly made was of tuberculous adenitis in those cases in which thyroid tumor was not present, carcinoma of the thyroid with metastatic extension in those in which thyroid tumor was present. In many of the latter cases, a double diagnosis was made of adenomatous goiter together with cervical adenopathy, lymphoblastoma, adenitis, and so forth. In 16 cases there were symptoms of pressure on surrounding tissue but they were not of help in arriving at correct diagnoses.

The "aberrant thyroid" tumor consisted of multiple nodules in 36 of the 54 cases, and of a single mass in 18. The growth was situated deep to one or the other sternocleidomastoid muscle in 50 per cent, in the posterior triangle of the neck in 27 per cent, in the submaxillary triangle in 19 per cent, and in the carotid triangle in the remainder of the cases. Before operation, the average duration of the tumor had been 5 years; the duration exceeded 10 years in 7 of the cases in which the lesion was malignant. Recurrence of the tumor usually took place from 6 months to a year after operation, but in 5 cases there was a delay of more than 5 years. Ten patients, 18.5 per cent,

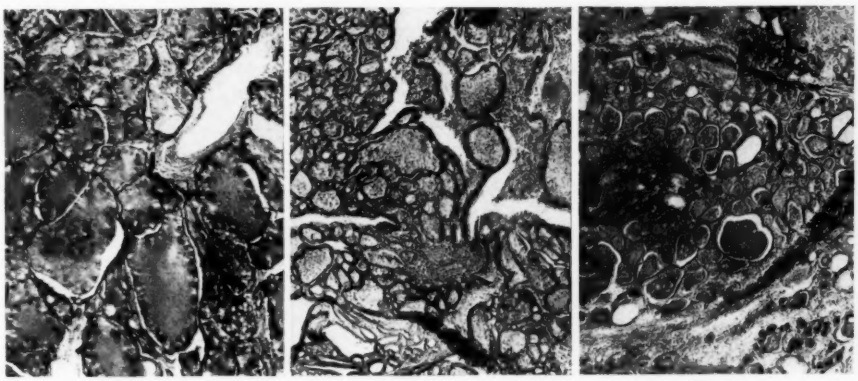

Fig. 1. Fig. 2. Fig. 3.

Figs. 1, 2, and 3. Lateral aberrant thyroid tumors in the 3 cases in our series in which the growths were benign. Sections from all three are indistinguishable from sections of colloid adenoma.

died of carcinoma of the thyroid gland subsequent to removal or biopsy of a malignant "aberrant thyroid"; in 4 cases the survival period varied from 11 to 19 years. One patient lived for 9½ years subsequent to the appearance of pulmonary metastatic lesions a year after removal of the "aberrant thyroid." It is apparent, therefore, that malignant "aberrant thyroids" are very slow-growing on the average, but that they eventually may cause death.

Of the 54 patients 3 had "lateral aberrant thyroid tumors" which, on microscopic examination, proved to be benign (Figs. 1, 2, and 3). In 2 of these cases a large, nodular goiter was associated with the "aberrant" thyroid tumor, which in each instance was situated immediately above one or the other superior thyroid pole. In the third case, the "aberrant" tumor was situated at the angle of the jaw on the right side and had been present for 30 years without change in its size. There was no direct connection between the thyroid tumor and the "aberrant" tumor in any of the 3 cases; in each case, microscopic examination revealed that tumors were composed of colloid and fetal adenomatous thyroid tissue without evidence of cellular undifferentiation, mitosis, vascular invasion, or lymphoid tissue.

The 51 other "aberrant" thyroid tumors on microscopic examination proved to be malignant. In 31 cases, 60 per cent, there was an associated tumor of the thyroid, the malignant nature of which was confirmed by microscopic examination, by obvious inoperability, or by subsequent death of the patient from carcinoma of the thyroid. In each of these 31 cases the thyroid tumor and the "aberrant" tumor were on the same side of the neck, and in each of 19 of these cases in which specimens from both tumors were obtained, the structure of the tumors was histologically identical (Figs. 4 to 9). All of the 10 deaths in the series of 54 cases occurred in this group, and of 24 patients who experienced recurrence of tumor, 19 had both thyroid and "aberrant" tumors.

Of the 20 patients remaining, 3 had associated thyroid tumors, the pathological nature of which was doubtful clinically and was not determined by operation. In the 17 other cases clinical evidence of thyroid tumor was not observed; in 13 of these cases, attempt was not made to examine the thyroid at operation, but in 4 the gland was exposed and, since it seemed normal on palpation, was left undisturbed by the surgeon. In the whole group of 20 cases, recurrence took place in 4, of which 1 was in the group of 4 in which the thyroid gland was left undisturbed at operation. The thyroid gland was not involved later in any case, nor was death related to the disease in any case. At the time this paper was written 10 patients were living and free from recurrence of tumor; 4 had had one recurrence; 1 died of natural causes; reports were not received from the 5 others after dismissal.

In 38 of the 51 cases of malignant tumor, 75 per cent, the pathologist on examination of the "aberrant" tumor made a diagnosis of papillary adenocarcinoma. Of these tumors, 20 were classified as of grade 1, 18 as of grade 2; the grading was on a basis of 1 to 4, in which grade 1 is the least malignant and grade 4 the most malignant. In 12 of the tumors of grade 2 the papillary tissue was mixed with nonpapillary, solid carcinomatous tissue. The tumors of grade 1 were distinguished by the long, arborizing processes which projected from

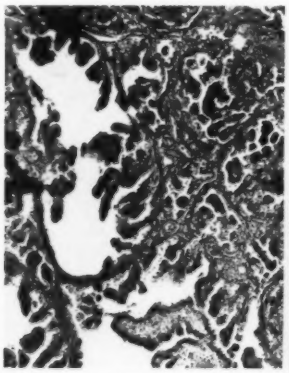

Fig. 4.

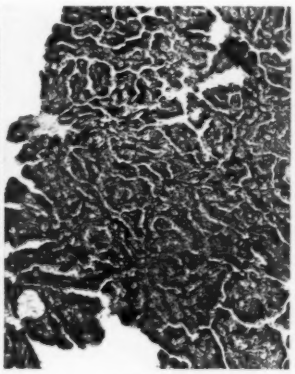

Fig. 5.

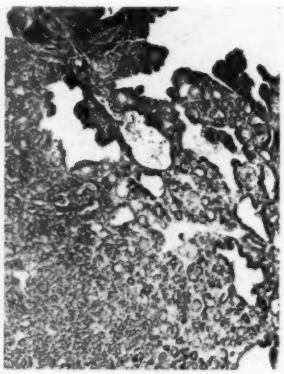

Fig. 6.

Fig. 7.

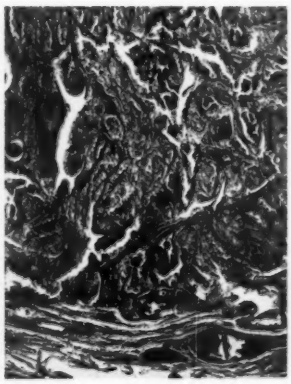

Fig. 8.

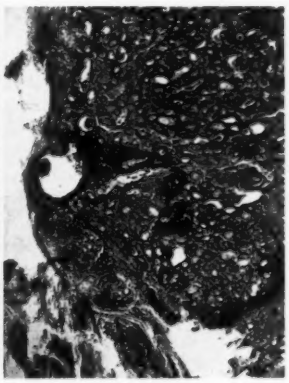

Fig. 9.

Figs. 4 to 9. The pathological characteristics of papillary lateral aberrant thyroid tumors (Figs. 4, 5, and 6) and of the tumors in the corresponding thyroid lobe compared (Figs. 7, 8, and 9). Papillary adenocarcinoma, grade 1 (Figs. 4 and 7); pure papillary adenocarcinoma, grade 2 (Figs. 5 and 8); mixed papillary and nonpapillary adenocarcinoma, grade 2 (Figs. 6 and 9).

thin cystic walls into large spaces, the lining epithelium being one layer thick for the most part; in the tumors of grade 2, the processes were thick and stubby, were covered by two or more layers of epithelial cells, and usually projected into small cystic spaces which often were surrounded by sheets of less well-differentiated cancer cells. Evidence of mitosis was present in all specimens of the papillary group and was observed more frequently in the tumors of grade 2. Prolonged search was required to discover mitotic figures in the majority of tumors of grade 1. Vascular invasion could not be demonstrated in any tumor of grade 1 and in only a few of the tumors of pure grade 2, but in the majority of the tumors invasion of the capsule or the capsular lymphatics was evident. The majority of the tumors of mixed grade 2 revealed vascular, capsular, and lymphatic invasion (Figs. 10, 11).

The 13 other malignant "aberrant" tumors were nonpapillary adenocarcinomas and all were associated with thyroid tumors. They were graded from 1 to 4 according to the degree of cellular undifferentiation, the tumors of grade 4, or diffuse carcinomas, being totally undifferentiated. Evidence of mitosis was extremely difficult to find in the tumors of the first three grades but was abundant in those of grade 4. Invasion of the vessels was discovered in all the tumors of higher grade and in most of those of grade 2, but was lacking in some of the tumors of grade 2 and of grade 1. Capsular and lymphatic invasion was less prominent in the lesions of this group than in those of the papillary group, but nevertheless was well

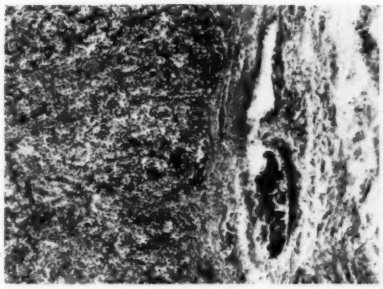

Fig. 10.

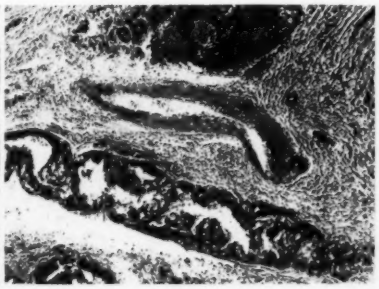

Fig. 11.

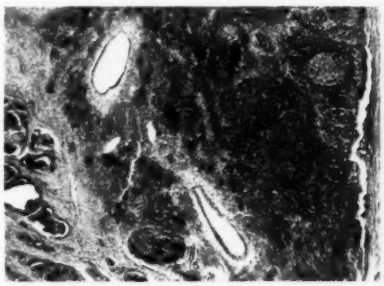

Fig. 12.

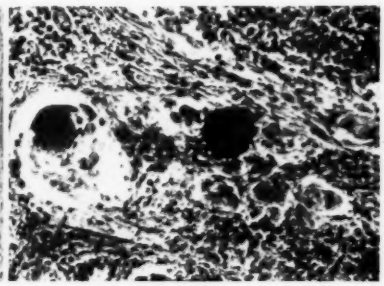

Fig. 13.

Figs. 10 to 13. Histological evidence of malignancy in lateral aberrant thyroid tumors; tumor thrombus in a capsular vein (Fig. 10); capsular lymphatic distended by tumor tissue (Fig. 11); typical lymph node structure with carcinomatous metastasis (Fig. 12); tumor cells lying in a peripheral sinus of a lymph node (Fig. 13).

marked. The tumors of grade 4 invaded all the tissues surrounding them, as would be expected.

Twenty-eight, 55 per cent, of the malignant "aberrant" tumors contained lymphoid tissue, usually in the form of a shell around the cancerous tissue with finger-like processes extending into it (Fig. 12). Often peripheral sinuses were seen between lymphoid tissue and capsule; at times these contained cancer cells (Fig. 13). Only one of the thyroid tumors contained lymphoid tissue.

The operative procedures used in the treatment of these 54 patients are given in Table I.

An analysis of the results was made, from the standpoint of recurrence of tumor, according to the completeness of the operative procedure, and as to whether or not postoperative treatment by radiation was given. Removal of all grossly involved structures, including the corresponding thyroid lobe if it, too, was involved, constituted a complete procedure. Of 21 cases in which complete removal of the tumor was followed by radiation, recurrence took place in 8, or 38 per cent. In 16, in which removal was incomplete but was followed by radiation, recurrence took place in 10, or 62.5 per cent. In 12 cases of complete removal, without radiation, recurrence took place in 5, or 42 per cent, an incidence equal to that in the first group. Therefore, among those patients who received postoperative treatment by radiation, complete removal of the grossly involved structures,

TABLE I.—OPERATIVE TREATMENT OF SO CALLED ABERRANT THYROID GLANDS

	Cases
1. Excision of aberrant thyroid tumor	17*
2. Dissection of lymph nodes of neck:	
Partial	3*
Radical	4
3. Hemithyroidectomy combined with:	
Excision of aberrant thyroid tumor	4
Dissection of lymph nodes, partial	3
Dissection of lymph nodes, radical	2
4. Removal of specimen of aberrant thyroid	11
5. Total and subtotal thyroidectomy with:	
Excision of aberrant thyroid tumor	3
Dissection of lymph nodes, radical	3†
6. Hemithyroidectomy subsequent to excision of aberrant thyroid tumor or dissection of lymph nodes	3
7. Removal of thyroid isthmus	1†
Total	54

*In one case in each group, hemithyroidectomy was done before patient came to clinic.

†In one case biopsy of aberrant thyroid tumor was performed before patient came to clinic.

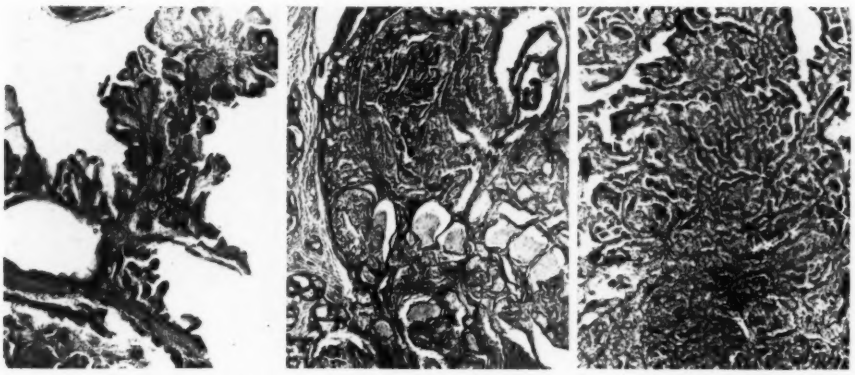

Fig. 14. Fig. 15. Fig. 16.

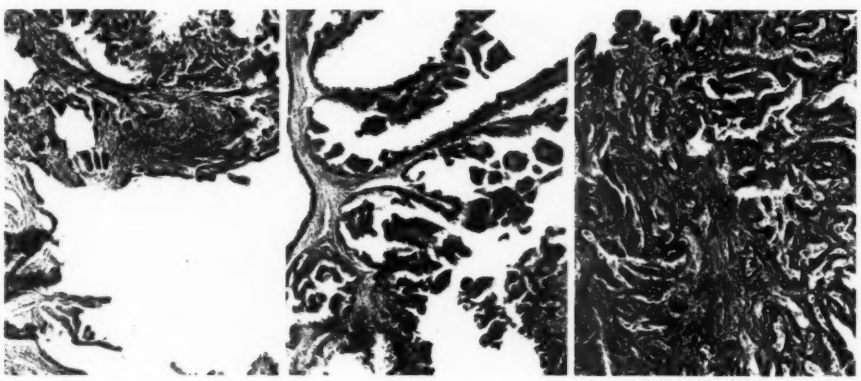

Fig. 17. Fig. 18. Fig. 19.

Figs. 14 to 19. Evidence confirming the lethal power of papillary tumors of thyroid tissue; all 6 patients represented in Figures 14 to 19 died of carcinoma of the thyroid. Figures 14, 15, and 16 were taken from the "lateral aberrant thyroids" in cases in the first series. Figures 17, 18, and 19 were taken from the thyroid tumors of patients in the second series. Papillary adenocarcinoma, grade 1 (Fig. 14); pure papillary adenocarcinoma, grade 2 (Fig. 15); mixed papillary and nonpapillary adenocarcinoma, grade 2 (Fig. 16); pure papillary adenocarcinoma, grade 1, of the type commonly called benign papillary cystadenoma (Figs. 17, 18, and 19).

both thyroid and "aberrant thyroid," afforded a better prognosis for cure. All 10 of the deaths occurred in the group in which the surgical procedure was incomplete, in spite of the fact that recurrence developed in 40 per cent of the cases in which removal was "complete."

Recurrence took place in 15 of the 38 cases of papillary tumor (40 per cent) and in 9 of the 13 of nonpapillary tumor (70 per cent); 7 of the 10 deaths occurred in the latter group. Of the 3 deaths in the papillary group, 2 were caused by tumors unmixed with nonpapillary elements (Figs. 14, 15, and 16). Thus it becomes clear that although the papillary tumors are clinically much less malignant than the nonpapillary, their power to cause death cannot be questioned even when nonpapillary carcinomatous elements are lacking. Confirmatory evidence is furnished by the photomicrographs in Figures 17, 18 and 19. Treatment by radiation would seem to be of questionable value unless the surgical procedure was "complete" and even then it is not strikingly effective.

ANALYSIS OF 15 CASES OF PAPILLARY CARCINOMA OF THYROID WITH REGIONAL METASTASIS AND COMPARISON WITH CASES OF ABERRANT TUMOR

Comparing with the cases in the series described previously those 15 cases in which papillary carcinoma of the thyroid with regional metastatic extension was conceded to be the correct diag-

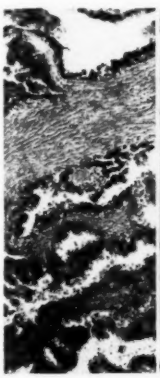

Fig. 20.

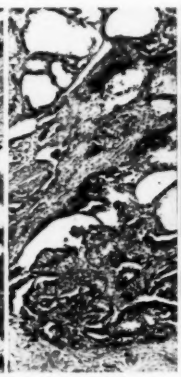

Fig. 21.

Fig. 22.

Fig. 23.

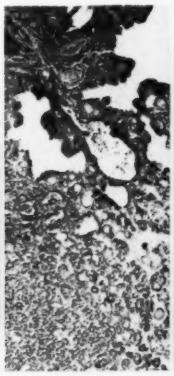

Fig. 24.

Fig. 25.

Figs. 20 to 29. Lateral aberrant thyroid tumor (Figs. 20, 22, 24, 26, and 28) and the tumor of the corresponding thyroid lobe (Figs. 25, 26, 27, 28, and 29) compared in 3 cases (Figs. 20 and 21, 22 and 23, 24 and 25) in which the thyroid tumor was discovered by the pathologist after its removal, and in 2 other cases (Figs. 26 and 27, 28 and 29) in which it was discovered by the surgeon at operation.

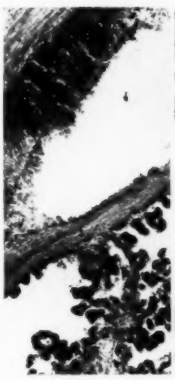

Fig. 26.

Fig. 27.

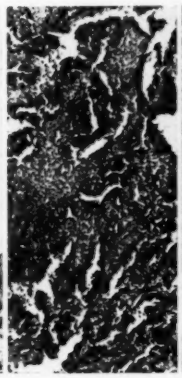

Fig. 28.

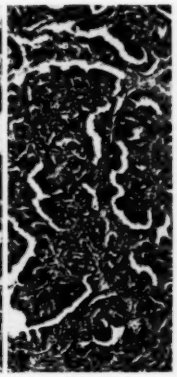

Fig. 29.

nosis, we found that the metastatic nodes, if not bilateral, were always on the same side as the involved thyroid lobe and that their histological structure invariably was identical with that of the thyroid carcinoma. There was definitely lymphoid tissue surrounding the malignant regions in 9 of the 15 representative metastatic nodules, 60 per cent, an incidence which compares almost exactly with that in the series of so called lateral aberrant thyroid tumors. Lymphoid tissue was present in the thyroid tumors in 2 cases. Vascular invasion was evident in 1 of the 7 tumors of grade 1 and in 7 of the 8 tumors of grade 2. The frequency of mitosis and of capsular and lymphatic invasion closely approximated that of "aberrant thyroid" tumors.

It is obvious, therefore, that the cases of the 2 series are indistinguishable from one another pathologically and that the separation out of some of the tumors as examples of "lateral aberrant thyroid tumor" was purely empirical according to the relative degree of prominence of the clinical history and findings of the "aberrant" or the thyroid tumor. The frequent insignificance of the associated thyroid tumor is illustrated by the fact that in 4 cases the thyroid tumor was not discovered until the gland was exposed at operation; in 3 others, the surgeon removed the homolateral thyroid lobe, even though it looked and felt normal, because the pathologist's report of the excised cervical tumor was papillary adenocarcinoma of the thyroid type, and in each a tiny and identical tumor was found buried inside the lobe. In no case in which the homolateral lobe was removed did the pathologist fail to find in that lobe a tumor identical in structure with that of the "aberrant thyroid." The following report of cases serves to illustrate the points mentioned in this paragraph:

Case 1. (Figs. 20 and 21.) A man, aged 32 years, who came to the clinic complaining of dysphagia, had had two tumors, one under the right sternocleidomastoid muscle and one at the angle of the jaw, for 10 years. In the 5 months previous to admission he had noticed rapid increase in size of the masses. A clinical diagnosis of Hodgkin's disease

Fig. 30.

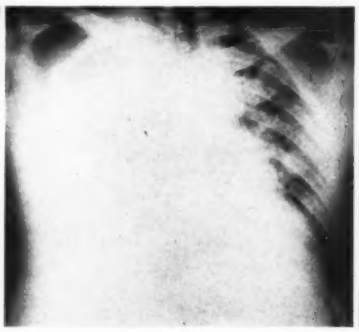

Fig. 31.

Fig. 32.

Fig. 33.

Fig. 34.

Fig. 35.

Figs. 30 to 35. Histological and roentgenological evidence of distant metastasis from pure and mixed papillary tumors of thyroid tissue. Fig. 33 shows a metastatic involvement of bregma of skull by papillary adenocarcinoma, grade 1. Figures 30, 31, and 32 show metastasis to the mediastinum, to the lungs, and to the lungs, respectively, from mixed papillary and nonpapillary adenocarcinoma, grade 2. Figure 34, metastasis to the lungs from a nonpapillary adenocarcinoma, grade 2, with papillary elements. Figure 35, histological section of a scalp nodule secondary to a pure papillary adenocarcinoma, grade 2. Figures 31, 32, 34, 35, all represent so called lateral aberrant thyroid tumors.

was made and operation was performed for excision of the tumors; the thyroid was not examined surgically. The pathologist at first reported that the tumors were branchial cystadenomas but later changed diagnosis to papillary adenocarcinoma, grade 1. Treatment by radiation not given.

The patient returned 9 months later with recurrence under the right sternocleidomastoid muscle and at the angle of the jaw on the right and on the left side. Right partial block dissection was done. The pathologist reported that the tumors were adenocarcinoma, grade 1, probably metastatic from the thyroid. Although the thyroid felt and looked normal, because of the pathologist's diagnosis of adenocarcinoma, the right lobe was resected. Microscopic examination revealed in the lower pole a tiny nodule of meaty looking tissue, which proved to be papillary carcinoma, grade 1. The nodule at the angle of the jaw on the left side was not removed. The "aberrant" tumor was cystic, contained lymphoid tissue, and mitotic figures were evident. The thyroid tumor was solid and there were occasional mitotic figures. The metastatic lesions were cystic, gave evidence of capsular and lymphatic invasion, and contained lymphoid tissue. All the growths were simple papillary carcinomas arising in adenomas, except, in the metastatic nodes, for occasional regions which were suggestive of nonpapillary adenocarcinoma.

The patient received treatment by radiation. Two months later recurrence had not taken place.

Case 2. (Figs. 22 and 23.) A woman, aged 37 years, on examination at the clinic had had a single tumor under the right sternocleidomastoid muscle for 2 months. The patient stated that the tumor fluctuated in size and that when it was large it caused dyspnea by pressure on the trachea. A diagnosis of branchial cyst was made clinically, and operation was performed for removal of the growth. The thyroid appeared normal on surgical exploration, but because of the pathologist's report that the cyst was a papillary carcinoma, right hemithyroidectomy was done, and in the extreme tip of the superior pole of the lobe there was found a tiny nidus of carcinomatous tissue. Microscopic examination of the specimen revealed mixed papillary and nonpapillary carcinoma, grade 2, of the thyroid, with regional metastatic lesions. The cervical cystic tumor contained

frequent mitotic figures and showed capsular invasion; lymphoid tissue was not found. The thyroid tumor was composed of mixed solid and cystic tissue, contained many mitotic figures, and gave evidence of vascular, capsular, and lymphatic invasion.

Six months later the patient was subjected elsewhere to right radical block dissection of tumors of the neck and afterward was treated by radiation. Seven years after her first operation she reported that she was in good health, free from recurrence.

CASE 3. (Figs. 24 and 25.) A woman, aged 37 years, came to the clinic because of gradually increasing tumor of 4 years' duration situated under the right sternocleidomastoid muscle. Clinical diagnosis was made of cervical adenopathy, and the tumors were excised. The pathologist reported that the growths were papillary carcinoma. Although the thyroid on surgical exploration apparently was normal, the surgeon was doubtful and resected the right lobe, in the upper pole of which were found two small nodules that proved to be carcinomatous. Microscopic study revealed mixed papillary and nonpapillary adenocarcinoma, grade 2, of the thyroid with regional metastatic extension. Patient received radiation treatment.

Five months later the patient returned with recurrence of tumors under the right sternocleidomastoid muscle. Radical block dissection was made and was followed by radiation. The pathologist's report was identical with that made 5 months previously. The "aberrant" tumor was solid, contained abundant mitotic figures and evidence of vascular invasion; lymphoid tissue was not present. The thyroid tumor was of the same type but in addition showed evidence of capsular and lymphatic invasion. The recurrent tumor which was removed at the second operation possessed all the features of both the "aberrant" tumor and the thyroid tumor and contained lymphoid tissue.

Nine years after first operation the patient living and well.

CASE 4. (Figs. 26 and 27.) A man, aged 24 years, had had multiple tumors of the right side of the neck, under the sternocleidomastoid muscle and at the angle of the jaw, for 10 years. They gradually had increased in size. When operation was performed for excision of the tumors, surgical exploration of the thyroid revealed a tumor in the right lobe, and right hemithyroidectomy was done. The pathologist reported papillary adenocarcinoma, grade 1, of the thyroid with regional metastatic extension. Both the thyroid tumor and the metastatic tumors were cystic and contained occasional mitotic figures, lymphoid tissue was present, and there was evidence of capsular and lymphatic invasion. The papillary carcinoma arose from an adenoma. The lymphoid tissue in the thyroid was a nodule extrinsic to the encapsulated tumorous tissue and was not invaded by it. Patient later received treatment by radiation.

Eight years afterward the patient returned to the clinic because of recurrence of tumors under the left sternocleidomastoid muscle; he again received treatment by radiation. Two years later it was reported tumors were still present. The patient did not return for further treatment.

CASE 5. (Figs. 28 and 29.) A woman, aged 22 years, came to the clinic because of multiple tumors of the neck and at the angle of the jaw on the right side. The growths had been present for 2 years and gradually were increasing in size. Physical examination revealed that the tumors in the neck were under the sternocleidomastoid muscle. Diagnosis was made of tuberculous adenitis. Biopsy at the time of surgical intervention revealed the presence of papillary carcinoma; a right radical block dissection of the tumors was made and after exploration of the thyroid, the right lobe, which was enlarged slightly, was removed.

The pathologist reported papillary and nonpapillary carcinoma, grade 2, of the thyroid with regional metastatic extension. The specimen of tissue removed for biopsy was solid and, on microscopic examination, was found to contain occasional mitotic figures. The thyroid tumor and metastatic tumors were solid and mitotic figures were present with evidence of capsular, vascular, and lymphatic invasion. None of specimens contained lymphoid tissue.

Subsequent to operation the patient received treatment by radiation. Two months afterward recurrence of the tumors had not taken place.

CASE 6. (Figs. 4 and 7.) A girl, aged 18 years, registered because of the presence for 9 months of multiple tumors of the left side of the neck. On physical examination the growths proved to be under the left sternocleidomastoid muscle and in the left posterior triangle. Three weeks before the patient came to the clinic, biopsy had been performed elsewhere of one of tumors in posterior triangle, and pathologist's report papillary carcinoma.

A clinical diagnosis was made of cervical carcinoma and at operation all the cervical nodules were removed. The thyroid was examined and apparently was normal. The pathologist reported the nodules as papillary adenocarcinoma, grade 1, probably metastatic from the thyroid. Treatment by radiation was not given.

The patient returned 1 month later with a recurrence under the left sternocleidomastoid muscle and a palpable tumor in the left lobe of the thyroid. Left radical block dissection and left hemithyroidectomy were done. Both tumors proved to be papillary adenocarcinoma, grade 1, identical with the nodules removed earlier. Microscopic examination of the "aberrant" tumor revealed solid tissue that contained occasional mitotic figures; lymphoid tissue was present and capsular invasion had taken place. The findings in thyroid tumor and metastatic nodes were the same except thyroid tumor contained no lymphoid tissue.

The patient received treatment by radiation; 9 months later she had remained free from signs of recurrence.

In 9 cases, the thyroid tumor did not become clinically detectable until some time after removal or biopsy of the "aberrant" tumor; in 3, the thyroid tumor was the first to appear. In 17 cases, as has been stated, a tumor in the thyroid gland never developed, even though there was recurrence of the "aberrant" tumor in the neck. All but 4 of the 17 patients received radiation and by this treatment a primary growth in the thyroid may have been destroyed. Believing, as we do, that all "lateral aberrant thyroids" are metastatic tumors from primary growths in the thyroid, the failure of appearance of a thyroid tumor in the last 4 cases must be attributed to the slow rate of growth which has been shown to characterize this type of carcinoma.

EVALUATION OF STUDY

It has been pointed out previously herein that some of the authors who believe in the "activated rest" theory of origin of "lateral aberrant thyroids" have expressed the opinion that physiological overstimulation of the constitutionally inferior tissue derived from the lateral anlagen causes to develop in that tissue papillary change which proceeds to malignancy. These men accept the view that the lateral components do form part

of the lateral thyroid lobes. In support of their opinion, they state further that carcinoma seldom, if ever, occurs along tract of median anlage.

It is well recognized that among adolescents physiological overstimulation of the thyroid in the presence of iodine deficiency, results in diffuse colloid goiter. Goiter of this type is devoid of any of the papillary elements which one would expect to find, according to these writers, if the lateral anlagen were constitutionally inferior. Furthermore, papillary carcinoma of the thyroid gland often involves a whole lobe uniformly, commonly stopping abruptly at the midline. Thus both median and lateral components are invaded similarly, the line of demarcation appearing to be based on direction of lymph flow. Probstein and Agress reported a case of papillary change in a nodule of thyroid tissue situated in the right side of the base of the tongue; the position of this nodule would indicate that it was derived from the median component. Such a case offers proof that papillary change is not limited to tissues derived from the lateral anlagen.

We have shown that the majority of the so called lateral aberrant thyroids occupy positions in the neck anatomically identical with the deep cervical lymph nodes and that 55 per cent of them present definite microscopic evidence of lymph nodal tissue; that is, in capsule, lymph follicles, and peripheral sinuses (Figs. 12 and 13) which have not been entirely destroyed by the malignant cells. It has been pointed out that some observers have expressed the opinion that such tissue is not indicative of metastatic infection of a lymph node but is characteristic of "lateral aberrant thyroid tissue." Yet in our series of cases we were unable to find any evidence of lymph nodal tissue in the thyroid tumors which, according to the same men, are derived from the same source as the "aberrant thyroids." Furthermore, photomicrographs of the developing median and lateral anlagen at the stage of budding out from the pharynx, reveal no lymphocytes associated with the thyroid epithelial primordium (34). In our opinion, it is impossible to distinguish microscopically metastatic lymph nodes from "aberrant thyroids" in the same or in different cases.

Tumors derived from the median anlage are found at its site of origin or along the path of its descent; if "lateral aberrant thyroid tumors" were really derived from the lateral anlagen, one would expect to find them situated also somewhere along the tract of the lateral anlagen from the pharyngeal wall to the thyroid. Weller showed that this tract lies between the carotid sheath and the thyroid lobe laterally and the trachea and esophagus medially. We have found that the majority of these "lateral aberrant" tumors lie superficial to or external to the carotid sheath. There is no record at the clinic of the finding of normal thyroid tissue elements lateral to the thyroid gland during the course of the routine microscopic examination of material removed in several thousand radical dissections of the neck performed for conditions other than cancer of the thyroid gland.

Lahey and others expressed the belief that the papillary thyroid tumors coexistent with many "aberrant thyroids" are metastatic from the latter into the thyroid. Mahorner and others showed that the direction of the flow of lymph in the thyroid gland is outward from the gland to the deep cervical nodes, the lymphatics of each lobe going to the nodes of their own side and not crossing over to the opposite side. In our experience, metastatic tumors discovered in the thyroid gland invariably have been blood borne, most commonly from a hypernephroma (27). Carcinomas of the tongue, lips, pharynx, and so forth, characteristically invade the cervical nodes but have rarely, if ever, been found to metastasize to the thyroid.

Because of the unusually slow growth in many instances, the contention has been made that these "lateral aberrant papillary tumors" are not malignant, that recurrence does not take place subsequent to their surgical removal, that they do not give rise to distant metastatic growths, and that they do not cause death. We believe that we have presented data that are convincing evidence that these low grade "lateral aberrant thyroid tumors" spread more commonly by way of lymphatic extension and invasion of the capsule than by vascular invasion, and that harmless looking papillary "cystadenomas" of the thyroid tissue, as well as the more complex mixed papillary tumors, may cause death (Figs. 14 to 19). Figures 30 to 35 illustrate the fact that not only tumors of mixed papillary and nonpapillary elements but also simple papillary tumors of thyroid tissue may give rise to distant metastatic lesions.

The following report of 2 cases will serve to emphasize that a patient with a "lateral aberrant thyroid tumor" together with grave metastatic extension such as to the lungs may live a long time and that a low grade tumor that has been present for years may bring about a fatal termination:

CASE 7. (Fig. 34.) A girl, aged 9 years, was brought to the clinic because of rapidly growing multiple tumors of 2 months' duration under the left sternocleidomastoid muscle; enlargement of the left lobe of the thyroid also had been noted for 2 months. The child was hoarse, and examination revealed that the left vocal cord was fixed. Diagnosis was made of cervical malignant disease. Biopsy of a left cervical node disclosed carcinoma, grade 2, in an adenoma,

metastatic from the thyroid. The tumor was solid, composed chiefly of nonpapillary elements with a few papillary elements. Mitotic figures were rare; vascular invasion had not occurred and lymphoid tissue was not present. The condition of the thyroid was inoperable. Treatment by heavy radiation was given.

A year and a half later pulmonary metastatic lesions developed, for which roentgen therapy was applied at repeated intervals. Eleven years after her first examination at the clinic the patient died of carcinoma of the thyroid with metastatic extension to the lungs.

CASE 8. A man, aged 28 years, had had multiple tumors in the right and the left posterior triangles for 14 years. The growths had increased in size in the 3 months previous to his admission to the clinic. For two years the left lobe of the thyroid had been greatly enlarged, the right lobe less so. Examination revealed that the left vocal cord was fixed. The clinical diagnosis was of lymphoblastoma. Biopsy of a left cervical tumor revealed papillary adenocarcinoma, which was diagnosed as metastatic from carcinoma primary in the thyroid. The tumor was cystic, contained occasional mitotic figures, capsular invasion had occurred, lymphoid tissue was not present. The condition of the thyroid was inoperable. The patient was treated by intensive radiation.

As the result of repeated application of radiation, the cervical tumors remained stationary for 14 years, when the patient died from carcinoma of the thyroid.

In our opinion, the most likely explanation of the presence of benign thyroid tumors (Figs. 1, 2, and 3) in the side of the neck, separate from the thyroid, is the pinching off of adenomatous masses from a large nodular goiter by surrounding structures, especially muscles; these masses then drift laterally or upward (24, 28). Analogous cases have been reported in which large adenomas were found in the thorax completely separated from the mother tumor.

CONCLUSIONS

1. So called lateral aberrant thyroid tumors are nearly always metastatic extensions to the deep cervical lymph nodes from a primary carcinoma in the homolateral lobe of the thyroid gland.

2. Seventy-four per cent of these tumors are papillary adenocarcinomas and spread by lymphatic extension.

3. Sixty per cent of "lateral aberrant thyroid tumors" are associated with thyroid tumors of identical structure which always are situated on the same side.

4. The "aberrant" tumors should be treated by radical block dissection of the neck and removal of the corresponding thyroid lobe, whether or not a tumor can be felt or seen in that lobe at the operating table.

5. Complete removal of all nodes and thyroid tissue known to be involved is essential if recurrence is to be prevented. Treatment by radiation is of questionable benefit unless surgical removal of the diseased tissue has been complete.

6. Following complete surgical removal the prognosis is good in cases of papillary and low grade nonpapillary carcinomas because the rate of growth of these lesions is very slow and these tumors do not commonly invade surrounding structures; in the inoperable or neglected cases, they may have little effect on the patient's general health for years but they eventually may cause death.

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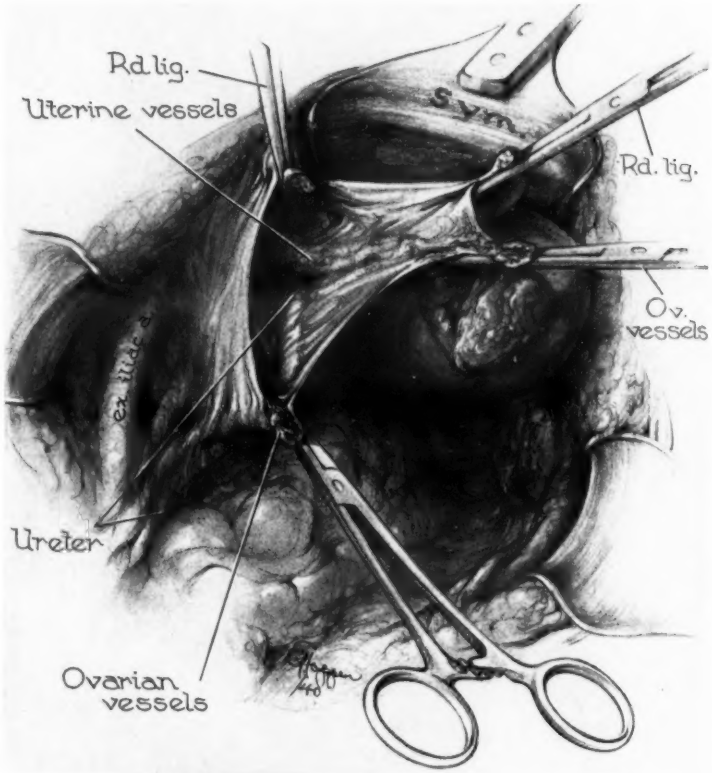

Fig. 1.

Fig. 2.

The Removal of the Regional Lymph Nodes in Cancer of the Body of the Uterus.—H. W. Johnston.

THE REMOVAL OF THE REGIONAL LYMPH NODES IN CANCER OF THE BODY OF THE UTERUS

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IT is a recognized surgical fact that any operation for cancer is incomplete unless the regional lymph nodes are removed. The lymph vessels that drain the body of the uterus are found in the suspensory ligament of the ovary, along the uterine vessels, and the round ligament. The nodes lie along the uterine, external, and common iliac vessels. An inconstant node is found at the internal inguinal ring. An operative procedure embodying these principles is presented.

From the Department of Obstetrics and Gynæcology, University of Toronto, and the Gynaecological Service of the Toronto General Hospital.

The technique of the operation. The patient is placed in the lithotomy position, and the vagina is thoroughly cleansed and disinfected. A catheter is passed. The external os is oversewn. This pre-

Fig. 3.

vents soiling of the field with malignant cells when the uterus is being removed.

The patient is now changed to the Trendelenburg position and the abdomen is opened. The round ligament is identified at the internal inguinal ring, clamped, and divided. The ovariopelvic ligament containing the ovarian vessels is clamped and divided. The ureter is very superficial at this point, and should be identified before the forcep is applied. The uterus is firmly drawn to the opposite side by traction on the two forceps (Fig. 1). The other forceps are separated and the broad ligament is opened up widely. This is carried out by inserting two fingers between the leaves of the broad ligament and incising the anterior fold of peritoneum, outside and parallel to the ovarian vessels (Fig. 2). The cellular tissue is brushed aside by blunt and scissor dissection. The regional nodes lying along the uterine, external, and common iliac vessels are removed (Fig. 3). A similar procedure is done on the opposite side.

Pan hysterectomy is now performed. Since the ureter is discernible at all times it is never injured. This preliminary anatomical dissection also makes the hysterectomy easier, safer, and is much more radical.

THE DIAGNOSIS AND MANAGEMENT OF INCARCERATED AND STRANGULATED FEMORAL HERNIA

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THERE has been a recent revival of interest in the treatment of incarcerated and strangulated femoral hernia. The hope of lowering the prevailing very high mortality rate seems to have furnished the incentive. The more favorable outlook, which has resulted from advances in the management of most forms of intestinal obstruction, has not been shared by those patients in whom the obstruction has been due to incarceration or strangulation of a femoral hernia. In a recent article, Dunphy calls attention to the seriousness of this condition and lists three factors which he believes have contributed to the high mortality rate: (1) delay in treatment; (2) the advanced age of the patients; (3) improper surgical management.

DIAGNOSIS

Delay in treatment is often due to error in diagnosis, and this is frequently the result of failure to examine for a mass in the femoral region in the presence of preobstructive gastrointestinal symptoms, or failure to appreciate the significance of a femoral mass when it is noted.

Dunphy points out that the diagnosis of a strangulated femoral hernia usually can be established clinically if it is given due consideration. Whenever a patient, especially a woman past middle life, complains of unexplained gastrointestinal symptoms, obstipation, and particularly abdominal pain and vomiting, the possibility of a strangulated femoral hernia should be considered. A proper appreciation of these remarks will prove to be the first step toward a reduction of the prevailing high mortality rate.

One of the most common causes of intestinal obstruction is incarceration of abdominal contents in a hernial sac. Examination, therefore, of the site of the hernial rings is necessary to make a diagnosis, because local pain may be so mild that it does not direct attention to the seat of the trouble. The mass is commonly small in size and for this reason, in some instances, the patient or the surgeon may fail to appreciate the relation between the abdominal symptoms and the unobtrusive mass present in the groin.

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The anatomical relations of the sac in a femoral hernia are such that once the sac has appeared in the groin it is seldom replaceable into the abdomen, even by manipulation. The narrow neck of the sac and the small size of the femoral canal provide circumstances which occasionally result in strangulation of the sac alone (Figure 1, a and b). It may be difficult at times to differentiate this condition from strangulation of the contents of the sac. The relation of the sac to its contained structures is such that incarceration of the contents of the hernial sac can occur with relative ease (Fig. 1).

Acutely inflamed lymph nodes in the groin in an elderly individual may be confused with a strangulated femoral hernia (Fig. 2). This is due to the similarity of the constitutional and local disturbances in both conditions.

The differential diagnosis of a femoral hernia from an inguinal hernia can be made by noting the relation of the swelling in the groin to the pubic spine. In femoral hernia the neck of the sac is always lateral to the pubic spine, while in the inguinal hernia the sac makes its exit from the abdominal wall above or medial to the pubic spine. This difference in the site of exit from the abdomen usually can be seen on inspection while the patient is standing and bearing down to increase the intra-abdominal pressure. In the recumbent position many inguinal hernias are spontaneously reduced and thus lose their physical manifestation. The sac of a femoral hernia, however, will persist in place, even though it is freed of its contents, and it can be palpated lateral to the pubic spine. When incarceration of contents occurs, the differentiation between an inguinal and femoral hernia usually can be made by noting the relation of the mass to the pubic spine (Fig. 3). In each instance the mass may lie in the femoral or inguinal regions, but in the femoral hernia all of the mass is lateral to the pubic spine.

We have felt that the study of a series of consecutive cases of strangulated femoral hernia, with the emphasis placed on certain important findings, should yield a better insight into the problems of diagnosis and management of such conditions.

TABLE I.—INCIDENCE OF INCARCERATION AND STRANGULATION IN FEMORAL HERNIAS, COOK COUNTY HOSPITAL, 1931–40, TREATMENT

Year	Cases	Incarceration	Reduced or not operated upon	Operated upon
1931–32	66	33	11	22
1933–34	86	50	13	37
1935–36	99	51	4	47
1937–38	88	56	15	41
1939–40*	65	35	9	26
Totals	404	225	52	173

*To April, 1940.

STUDY OF 225 CASES OF STRANGULATED OR INCARCERATED FEMORAL HERNIA

In a series of 404 patients with femoral hernia admitted to the Cook County Hospital during the past 9 years, it was found that in 225 (55.7 per cent) there was incarceration or strangulation of hernial contents at the time of admission (Table I). In 46 of these 225 patients nonoperative reduction of the contents of the hernial sac into the abdomen was possible. These patients were relieved of their symptoms. In 6 instances the hernia could not be reduced manually, and the patients died before operative reduction could be attempted. Some of these deaths could be attributed directly to complications incident to the strangulation of the hernial contents, while in other patients there was no direct relationship between the cause of death and the pathological condition of the hernia. One hundred and seventy-three of the 225 cases required and received urgent surgical care. Of these, 121 were females and 52 were males, distributed in age groups as listed in Table II.

NONOPERATIVE REDUCTION OF HERNIAL CONTENTS

In the 46 patients who had nonoperative manipulative reductions of their hernias, there were no failures to relieve the symptoms immediately. Many of these patients, however, returned at a later date for elective surgery.

The technique of nonoperative reduction is based on the anatomical configuration of the sac and its relation to the surrounding structures. Pressure directly against the fundus of the hernial mass is inclined to increase the difficulty of reduction, because this maneuver tends to increase the angulation of the sac which is usually present where it turns abruptly to pass under the inguinal ligament. Gentle stroking of the mass downward and slightly inward with the hand will decrease the angulation just mentioned, and if the patient is supported in a moderate Trendelenburg position, it will facilitate the reduction of the contents of the hernial sac (Fig. 4). It is inadvisable to persist too long or to be too vigorous in one's attempts to reduce a femoral hernia. The communication between the peritoneal cavity and the sac may be too narrow to allow replacement of distended bowel, edematous omentum, or viscera. There have been many reports of the rupture of strangulated, necrotic bowel by too vigorous manipulation.

TABLE III.—OPERATIVE MORTALITY RATE

Year	Operated	Died	Mortality rate per cent
1931–32	22	8	36.3
1933–34	37	8	21.6
1935–36	47	10	21.2
1937–38	41	10	24.3
1939–40	26	4	15.3

TABLE II.—DISTRIBUTION OF OPERATIVE CASES OF INCARCERATED AND STRANGULATED FEMORAL HERNIA BY AGE GROUPS

Age	Number operated upon	Age	Number operated upon
13 mos	1	51 to 60 yrs	33
10 to 20 yrs	1	61 to 70 yrs	42
21 to 30 yrs	3	71 to 80 yrs	35
31 to 40 yrs	14	81 to 90 yrs	5
41 to 50 yrs	38	92 yrs	1

Under 40 years of age—19 cases.
Over 40 years of age—154 cases.

OPERATIVE MORTALITY

In the patients operated on (173) there were 40 deaths, or 23.1 per cent (Table III). There was a striking correlation between the mortality rate and the duration of symptoms. Fifteen patients were operated on within 12 hours of the onset of symptoms and only 1 died, 6.6 per cent. In 25 patients on whom the operation was performed 1 week after the onset of symptoms there were 9 deaths, 36 per cent (Table IV).

TABLE IV.—MORTALITY RATE IN RELATION TO DURATION OF SYMPTOMS

Duration acute symptoms	No. cases	Deaths	Percentage
12 hrs	15	1	6.6
24 hrs	37	6	16.2
2 days	27	7	25.9
3 days	27	5	18.5
4 days	14	4	28.5
5 days	20	4	20.
6 days	8	2	25.
1 wk. plus	25	9	36.
Totals	173	40	23.1

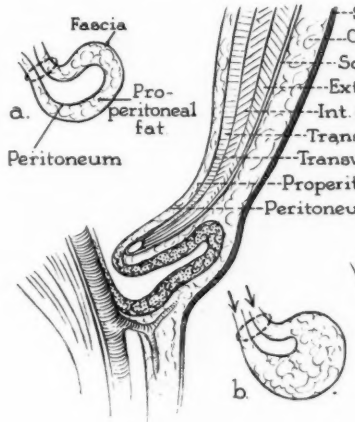


Fig. 1.

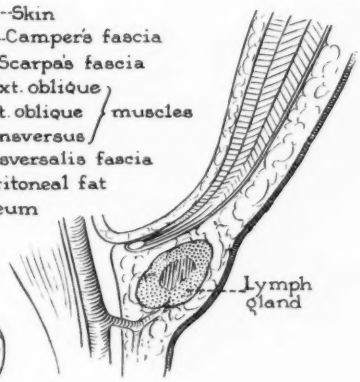


Fig. 2.

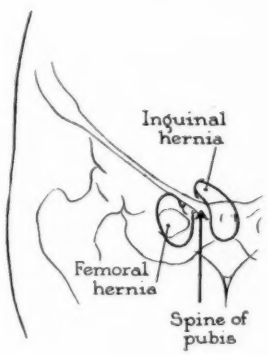


Fig. 3.

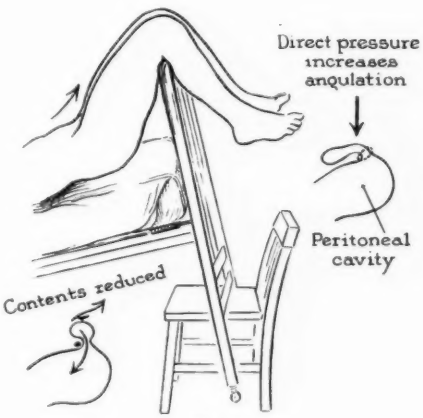


Fig. 4.

Fig. 1. The layers of the abdominal wall at the site of the femoral hernia. a and b, Variations in the extent of the fatty layer. Frequently this fat may be lobulated, giving the sac an irregular contour, instead of the smooth surfaces illustrated.

Fig. 2. An enlarged gland in the cribriform fascia may be mistaken for an incarcerated hernia, especially when suppuration of the gland is present.

Fig. 3. The relationship of the neck of the femoral hernia and the inguinal hernial sac to the spine of the pubis.

Fig. 4. Direct pressure against the sac makes the angle at the neck more acute and reduction is then rendered less likely. With the patient in the Trendelenburg position, stroking of the sac toward the knee may aid in the reduction of the contents.

SURGICAL PATHOLOGY

Contents of the sac. The contents of the sac in our reported cases varied as shown in Table V. In 10 instances there were no contents in the sac. In these the sac itself was either incarcerated in the femoral canal or strangulated, and the condition of the sac alone was responsible for the patient's complaint. These cases are the basis of a separate report which has recently been published (2).

When intestines were incarcerated in the hernial sac, an elevation of temperature was usually present (Table VI). A rapid pulse rate was an almost constant accompaniment.

TABLE V.—CONTENTS OF HERNIAL SAC

Contents	Cases
Omentum	44
Bowel	80
Omentum and bowel	39
Sac alone	10
Total	173

Fluid in the sac. The character of the fluid in the hernial sac found at operation is very definitely an indication of the seriousness of the condition. Eleven of the 17 patients who had a feculent fluid in the hernial sac died. A bloody fluid was present in 109 instances, in which there were 27 deaths. In 47 cases in which a serous fluid was present, there were but 2 deaths (Table VII).

MANAGEMENT OF BOWEL

There were 33 instances in which gangrenous bowel was resected, exteriorized, or invaginated. The incidence of each type of management and the death rate are listed in Table VIII. It is noteworthy that in the 11 cases in which exteriorization was done there were 9 deaths. In the 4 cases in which invagination of what appeared to be a devitalized portion of the bowel wall was done there were 2 deaths. Twenty of the 33 patients in whom devitalized bowel was present died (60 per cent). In the absence of devitalized bowel (140 cases) there were only 20 deaths (14 per cent).

OPERATIONS

There are many operations which have been described as suitable to the treatment of femoral hernia. Some of these have been suggested as particularly useful in the management of the incarcerated or strangulated femoral hernia. We should like to emphasize the importance of the early diagnosis and the prompt management of the incarcerated femoral hernia. These considerations seem to be of greater significance in the reduction of the prevailing high mortality rate than the technique of operation.

The illustrations in Figures 5 to 10 present a technique which we have employed. The incision is made in a vertical direction parallel to the femoral vessels directly over the neck of the sac (Fig. 5). This point is determined by placing the ring finger upon the pulsating femoral artery. The middle finger will then lie on the femoral vein and the index finger will point to the neck of the sac (Fig. 6). The incision extends above and below the inguinal ligament for the same distance and is usually about 3 inches long. Beneath the subcutaneous fat lies the femoral hernial sac. This is delivered onto the surface of the thigh and is immediately packed off with warm moist laparotomy pads. The sac is opened very cautiously on its anterior surface close to the neck and any fluid present is allowed to escape. The contents of the sac may be inspected and held with a warm moist pad so that they do not slip back into the peritoneal cavity unexamined (Fig. 7). One should never grasp the strangulated bowel with forceps of any kind for fear of tearing these friable loops. The inguinal ligament is clearly defined and retracted cephalad with a small ribbon retractor. The femoral vein is identified and retracted laterally. The pectineus fascia is cleared up to the femoral canal. The femoral canal is now enlarged by incising the lacunar ligament and, when necessary, the inguinal ligament may also be cut (Fig. 8). The lacunar ligament and the inguinal ligament adjacent to the pubic spine are always incised under direct vision so that injury to any vessel is unlikely. With the enlargement of the femoral canal the sac can be pulled out from beneath the inguinal ligament and the contents exposed. Devitalized bowel, if present, should be gently withdrawn until normal bowel is exposed. It then may be resected and the continuity of the intestinal canal re-established (Fig. 10). We prefer the end-to-end type of anastomosis. Omentum which is gangrenous or markedly thrombotic is excised and otherwise damaged

TABLE VI.—RELATIONSHIP BETWEEN TEMPERATURE AND PRESENCE OF BOWEL IN HERNIAL SAC

Temperature	Cases	Bowel present
98 to 99	62	30
99 to 100	62	45
100 plus	49	44

TABLE VII.—RELATIONSHIP BETWEEN FLUID FOUND IN SAC AND MORTALITY

Fluid	Cases	Deaths	Percentage
Serous	47	2	4.25
Bloody	109	27	24.7
Feculent	17	11	64.7
Totals	173	40	23.1

TABLE VIII.—MORTALITY RATES IN MANAGEMENT OF GANGRENOUS BOWEL

Management of gangrenous bowel	Cases	Deaths	Percentage
Resection with end-to-end anastomosis	13	8	61.5
Resection with side-to-side anastomosis	5	1	20.
Exteriorization of dead bowel	11	9	81.8
Invagination of necrotic site	4	2	50.
Totals	33	20	60.6

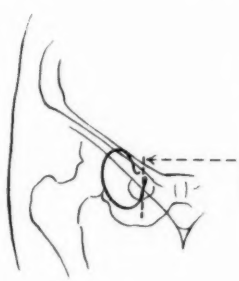
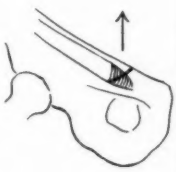


Fig. 5.

Fig. 6.

Fig. 7.



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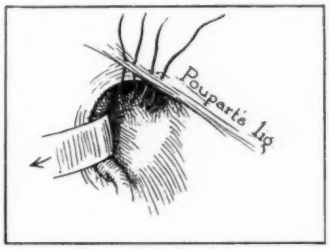

Fig. 9.

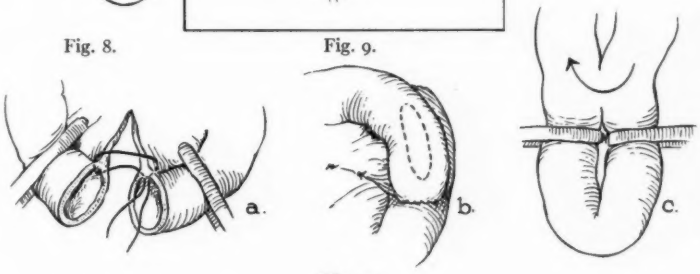

Fig. 10.

Figs. 5 to 10. A method of femoral herniotomy.

Fig. 5. Incision parallel to vessels immediately over neck of sac. The inguinal ligament lies beneath the middle of the incision, which is approximately three inches long.

Fig. 6. The neck of the sac is located by placing the ring finger upon the pulsating femoral artery and the middle finger will then lie on the femoral vein and the index finger will point to the neck of the sac.

Fig. 7. The sac is exposed and immediately "packed off" with warm moist pads. The contents are exposed and examined before reduction is done. This avoids the return of damaged bowel to the abdomen before examination is possible.

Fig. 8. Increasing the size of the femoral canal by cutting the distal attachment of the inguinal ligament at the spine of the pubis. The fascia is cut under direct vision. The fatty tissues behind it are pushed away with the finger. In the male the spermatic cord is retracted and protected from injury.

Fig. 9. The femoral opening is closed by suture of the pectineus fascia to the inguinal ligament.

Fig. 10. Methods of bowel management.

omentum is also removed. The femoral sac is then closed by ligation or transfixion at the neck and the stump guided along the femoral vein to a level which will not interfere with the approximation of Poupart's ligament to the pectineus fascia (Fig. 9). Closure of the external wound is usually made with interrupted sutures not too close together.

It appears from our analysis that exteriorization of the ileum or jejunum carries a high mortality rate. The serious consequences are due not only to the presence of dead bowel, but also to the

resulting changes in the blood chemistry and body tissues which ensue following the creation of an intestinal fistula. The avoidance of the fistula, if possible, is most desirable, and one should make every effort to restore the continuity of the intestinal tract.

SUMMARY

In a consecutive series of 404 patients with femoral hernia admitted to the Cook County Hospital from June, 1931, to April, 1940, 225 were incarcerated or strangulated on admission. Attempts at nonoperative reduction of the contents of the hernial sacs were successful in only 46 instances. Six patients died before operative reduction could be done. One hundred and seventy-three patients received surgical treatment. Sixty per cent of the patients with gangrenous bowel died (20 of 33 cases). In the absence of gangrene of the intestines the mortality rate was only 14 per cent (20 of 140 cases).

CONCLUSIONS

1. The diagnosis of incarcerated and strangulated femoral hernia must be made early if treatment is to afford a reduction in the prevailing high mortality rate.

2. Intestinal obstruction, partial or complete, due to a femoral hernia in elderly individuals, must be suspected, sought for and treated early, because gangrene of bowel jeopardizes recovery from this serious condition.

3. Restoration of intestinal continuity following bowel resection is more desirable than the establishment of an enterostomy.

4. In the operative treatment the sac should be opened and the contents inspected before the femoral canal is enlarged. This will avoid accidental reduction of the hernial contents before examination of questionably viable viscera is possible.

5. Enlargement of the femoral canal is accomplished by severing the lacunar and, if necessary, the inguinal ligament adjacent to the pubic spine.

6. A minimum of suture material should be used to approximate the inguinal ligament to the pectineus fascia, and the closure of the incision should be made with interrupted sutures not too closely spaced.

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ANESTHESIA IN CASES OF POOR SURGICAL RISK

Some Suggestions for Decreasing the Risk

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WHEN a patient who is classified as presenting a poor surgical risk comes to operation today, he stands a better chance of withstanding the effects of both the anesthesia and the operation than he did a few decades ago. Advances in many fields of medicine have helped to decrease the risk of operation and anesthesia in these cases. For instance, the use of insulin for diabetes, together with other methods of treatment, has reduced greatly the incidence of complications which accompanied surgical procedures on such patients. The preoperative management of patients who have thyrotoxicosis has reduced the morbidity and mortality rate accompanying thyroidectomy. Improved operative procedures have decreased the risk in certain fields, such as the present method of transurethral prostatic resection for prostatic hypertrophy.

Advances in the field of anesthesia and its related specialties have been of prime importance in the successful preoperative, operative, and postoperative management in cases of poor surgical risk. These advances are classified broadly as follows: (1) the evolution of less toxic anesthetic agents; (2) improved methods of administration of anesthetic agents; (3) the use of a combination of agents and methods, thereby decreasing the toxicity resulting from the use of a single agent, for instance, the so-called balanced anesthesia as previously described by one of us (Lundy, 25); (4) improved methods of administration of oxygen and other inhalants; (5) supportive measures during the operative and postoperative period and (6) special measures, such as the use of tracheobronchial aspiration after operation. Finally, the skill and versatility of the anesthetist must be considered as important contributing factors to the welfare of the patient for whom the risk of operation is great. The patient's life often depends more on the way a certain anesthetic agent is administered than on the effects of the anesthetic agent itself.

From the Section on Anesthesia, Mayo Clinic.
Read before the meeting of the Range Medical Society, Hibbing, Minnesota, July 22, 1941.

Various methods have been employed in grading the degree of risk which each patient presents.

Saklad (36), as a member of a committee of the American Society of Anesthetists, Inc. studied problems of classification of anesthetic data and suggested that the term "operative risk" be supplanted by the term "physical state." The reason for this suggested change was for the purpose of limiting many variable factors, such as the type of operative procedure, ability of the surgeon and anesthetist, and the type of anesthetic agent the patient will receive. On the basis of "physical state," 4 classes were made, with two additional classes for emergencies. In brief, the first 4 classes are as follows:

In class 1 are included cases in which organic pathological change is absent or the pathological process is localized and does not cause any systemic disturbance or abnormality; for example, any type of operation for fractures without shock or loss of blood or uncomplicated hernias.

In class 2 are included those cases in which a moderate but definite systemic disturbance, caused either by the condition that is to be treated by surgical intervention or which is caused by other existing pathological processes is present; for example, mild diabetes, mild acidosis, moderate anemia, or mild thyrotoxicosis.

In class 3 are included those cases in which severe systemic disturbance from any cause or causes is present. It is not possible to state an absolute measure of severity, as this is a matter of clinical judgment. For example, these conditions include complicated or severe diabetes, combinations of cardiac disease and respiratory disease, pulmonary tuberculosis associated with tachycardia or dyspnea, and severe accidental trauma associated with shock.

In class 4 are included those cases in which extreme systemic disorders already have become a threat to life regardless of type of treatment. For example, these disorders include cardiac decompensation, a combination of cardiovascular-renal disease with marked renal impairment and of an operation on a patient already in poor condition to arrest hemorrhage after much loss of blood.

One of us (Lundy) suggested a brief classification of operative risk as follows: grade 1, patients in such good physical condition that they will probably tolerate any anesthetic agent well; grade 2, cases of so-called average risk, in which the risk of the operation is greater than the risk of the anesthesia; grade 3, patients for whom the anesthetic agent must be selected with care, since, owing to pathological conditions, the risk of the anesthesia is as great or greater than the risk of the operation; and grade 4, patients who are in such serious physical condition that the use of any anesthetic agent is dangerous. For such patients, local infiltration may be used to control the pain but only half the concentration and half the usual amount of solution should be employed.

The risk of operation in a certain case can be evaluated intelligently only after all findings from physical and laboratory examinations are available. In certain cases, the effects of pathological lesions are so well marked that the risk is obviously poor. In others, there may be a number of obscure and less marked pathological changes which do not become apparent until the results of a complete examination have been obtained.

All anesthetic agents may be toxic to human tissue, but certain organs and tissues may suffer more acutely than others. The liver and kidneys usually are affected owing to their functions of detoxication and excretion (32). Certain anesthetic agents produce specific damage to certain organs, such as damage to the tissue of the liver by chloroform. When pre-existing damage to such an organ by some pathological process is present, the toxic effect of the anesthetic agent becomes more marked and results in greater inhibition of function. Therefore, in choosing the anesthetic agent for a patient who presents a poor surgical risk, the main factor to consider is to what extent the agent or agents will affect physiological processes already impaired. It is difficult and impractical to attempt to lay down general rules as to the choice of anesthetic agent for these patients, as each presents an individual anesthetic problem (13). The method of choice is one which will produce the least deleterious effects in the light of the existing pathological processes and which, at the same time, will be adequate for the anticipated operation. By the choice of the proper anesthetic agent, skillfully administered and preceded by careful preoperative preparation of the patient and accompanied by suitable supportive measures, it is possible to improve the status of his risk from one of doubtful outcome to one which offers him more than a reasonable chance of satisfactory convalescence and recovery (1, 37).

GENERAL FACTORS CONTRIBUTING TO THE PATIENT'S RISK

A few basic facts which can be ascertained from the physical and laboratory examinations usually will be all that are required in order to form a fair approximation of the risk of anesthesia and operation in a particular case. Important among these are the estimation of hemoglobin, the level of blood pressure, findings on urinalysis, degree of cardiac and renal sufficiency, and the general appearance of the patient in regard to nutrition, debility, and loss of weight. Although a more detailed examination may uncover further evidence of physiological abnormalities, such information may not be essential to the choice of the safest anesthetic agent. If these salient features are weighed and estimated carefully, it is not essential that facilities for a thorough laboratory examination be available. Some of the more ordinary factors to consider follow.

Age. Anesthesia and operation are not tolerated as well by patients at the extremes of life. The respiratory system of infants and young children is depressed easily by anesthetic agents. Debility and cardiovascular-renal disease may be complicating factors in the cases of aged persons. Miller observed that the mortality rate of surgical patients more than 50 years of age was eight times as great as that for patients less than 50. The need for supportive treatment should be anticipated for aged patients (15). Elderly patients fare better after operation if they are gotten up out of bed at the earliest possible time.

Habits. The mode of life of a patient has a bearing on the risk. Those who use tobacco excessively and have accompanying bronchitis are prone to respiratory complications after anesthesia and operation. Chronic alcoholics usually fare poorly under anesthesia and seem more susceptible to complications during the postoperative period. The same applies to drug addicts, since there are often accompanying nutritional and nervous disturbances.

Nervous system. Patients who are "high strung" usually are more difficult to anesthetize than those of more stolid type. Those who come to the operating room worried, frightened, and with the mental attitude that death is imminent or that they cannot survive the operation do not present a good risk and often have a stormy convalescence. Adequate preliminary medication and assurance are important therapeutic measures in these cases.

Toxic states. Toxemia, whether attributable to systemic or malignant disease, infections, or other causes, increases the gravity of the risk in direct proportion to the degree of toxemia present.

Debility. Patients who are frail, debilitated, underweight, and poorly nourished lack the reserve of robust patients to withstand the toxicity of anesthesia and the shock associated with the operation. The risk of operation on markedly debilitated patients is always high. The vital functions of these patients are depressed by even small doses of anesthetic agents and great caution must be observed to prevent overdosage. Prolonged vomiting is serious, since it leads to nutritional disturbances, decrease of glycogen in the liver, and to the more serious conditions of acidosis and ketosis. The other extreme, also serious, is alkalosis, which can be produced, among other conditions, by intestinal obstruction.

Obesity. Obese patients need not necessarily present a poor surgical risk, but by and large a patient who is grossly overweight does not have as good a chance of withstanding anesthesia and operation as one whose weight is nearer a normal figure. In the cases of obese patients, the operative manipulations often are more difficult and fatty infiltration of the cardiac muscle may be present, thereby lowering cardiac reserve and more or less inhibiting respiratory exchange.

HEPATIC FUNCTION

The liver and the state of its function have an important bearing on the anesthesia and its effect on the patient (31). One of the principal functions of the liver is its power of detoxification, including detoxification of certain anesthetic agents (3). In addition, the functions of the liver are inhibited and liver tissue is damaged by the action of certain anesthetic agents in the body. Bourne stated that with the exception of cyclopropane, all anesthetic agents may cause some impairment of hepatic function. The normally functioning liver, however, handles the strain imposed on it by anesthesia and operation well, provided its store of glycogen is adequate and anoxia is prevented. If its function has been impaired by toxemia and if nutritional disturbances have depleted its supply of glycogen, it then not only performs its normal functions poorly, but its vulnerability to further damage from the anesthetic agent is increased. The malfunctioning liver invariably has a low content of glycogen which always increases the risk from the anesthesia and operation. The most toxic anesthetic agent to hepatic tissue is chloroform, manifested by toxic changes in the lobules of the liver, degeneration and necrosis, leading to inhibition of function of varying degrees. For this reason, chloroform anesthesia has been largely abandoned. Divinyl ether anesthesia also may damage the liver, particularly if the state of anesthesia is prolonged, but not to the extent or with the frequency of that produced by chloroform. Ether anesthesia impairs the function of a normal liver slightly, causing diminution of its content of glycogen, hyperglycemia, and decrease in hepatic secretion, but normal function is soon resumed during the postoperative period. Cyclopropane has little, if any, deleterious effect on hepatic function, and the same is thought to be true in the case of the very short acting barbiturates.

The best means of protecting an impaired liver are diet high in carbohydrates in order to increase the content of glycogen of the liver before operation and the maintenance of adequate oxygenation during the anesthesia and after operation. In cases of obstructive jaundice, in which the prothrombin time is increased and postoperative hemorrhage is feared, treatment with vitamin K before operation is indicated (38). Allen and Livingstone stated that the early postoperative fall in prothrombin in cases of jaundice and biliary fistula seems to be caused primarily by the inadequate administration of vitamin K before the operation, rather than from anesthesia, operative trauma, or hemorrhage. Blood transfusions are also of value. Adequate oxygenation during anesthesia is of the utmost importance in protecting the liver against the toxic effects of anesthetic agents.

RENAL FUNCTION

Although the kidneys are affected directly by certain anesthetic agents, their function also is impaired indirectly as a result of the effect of the anesthesia and operation. Chloroform may produce direct damage to the renal epithelium. Ether anesthesia causes a marked decrease in urinary output, ending in almost complete suppression after an hour or more of anesthesia. Normal function is resumed in the first 24 hours after operation. Cyclopropane anesthesia also suppresses urinary output during anesthesia: this is followed by a compensatory increase in excretion after operation. Tribromethanol anesthesia also causes urinary suppression and Veal, Phillips, and Brooks have shown in rabbits that when even mild degrees of nephritis are present, the margin of safety with this type of anesthesia is small (41). If, at the time of operation renal damage has occurred, anesthetic agents which are toxic to renal tissue and tend to inhibit renal function will produce more drastic disturbances in these organs than if they were normal. Thus, renal insufficiency markedly increases the gravity of the patient's risk.

Indirect effects of the anesthesia and operation also have an important bearing on renal function. These effects, according to Beecher, depend on several things. A marked fall in blood pressure during operation can diminish and arrest urinary secretion. Asphyxia may cause constriction of the renal vessels, leading to diminished blood flow through the kidneys and decreased formation of urine. Owing to the resultant local anoxia, the glomerular epithelium is damaged and permits the passage of albumin, proteins, and blood. Loss of fluids and blood during the course of the operation also contributes to postoperative anuria. In cases of advanced nephritis the risk of operation is not good, and nephritis often is accompanied by arteriosclerosis, hypertension, and cardiac insufficiency, which further increase the gravity of the risk (33). In such cases, careful tests for renal function should be performed and the level of blood urea and nonprotein nitrogen should be evaluated. In the preparation of such patients for operation, the values for blood urea, creatinine, and nonprotein nitrogen should be reduced as far as possible by forcing fluids and intravenous therapy before operation. If these values stabilize readily to values not grossly abnormal, the patient may stand operation and anesthesia satisfactorily.

CARDIOVASCULAR SYSTEM

Cardiac insufficiency, if advanced and uncompensated, forms one of the gravest complications the anesthetist has to face. However, it is agreed among cardiologists that patients who have many types of cardiovascular conditions, provided that compensation is adequate and cardiac reserve is satisfactory, stand anesthesia and operation remarkably well (17). Patients who give the most concern are those who have advanced myocardial degeneration accompanied by circulatory insufficiency and marked dyspnea. Although a careful cardiovascular examination should be routine before any operation, a fair estimate of the patient's cardiac reserve may be obtained from information the patient can supply. If he does not have dyspnea or precordial pain, either with or without moderate exertion, and if he is able to carry on the usual activities of daily life, it is probable that his heart will stand the strain of anesthesia and operation. The risk increases in proportion to the extent with which his activities are limited by the cardiac condition. Hypertension itself does not increase the risk markedly, provided cardiac reserve is satisfactory. From a review of the literature, Woodbridge stated, "it is generally agreed that coronary occlusion, angina pectoris, congestive failure, and syphilitic aortitis carry high operative mortality; and that valvular heart disease and auricular fibrillation if uncomplicated by failure, and paroxysmal auricular flutter, fibrillation, or tachycardia do not add appreciably to the anesthetic or surgical risk."

RESPIRATORY SYSTEM

Disease of the lungs or of the respiratory passages obviously has an intimate bearing on the course of anesthesia, the complications that may arise and the degree of risk for the patient during and after operation. The effect is dependent on the site, nature, and extent of the lesion, to what extent the lesion will interfere with the supply of oxygen and its transportation to the body tissues and the elimination of carbon dioxide. There is also the added risk of the production of other pulmonary complications after operation as a result of the anesthesia and operation or the extension of those which existed before operation. Any pathological condition which lowers vital capacity to a marked degree increases the patient's risk. Moersch stated that the closer the vital capacity approximated tidal air, the graver was the risk. Examples of lesions which affect vital capacity are emphysema, abscess of the lung, tuberculosis, pneumonia, pleurisy with effusion, asthma, defects of the thorax, and also certain cardiac conditions, particularly mitral stenosis.

A reduction in vital capacity always calls for particular care in the maintenance of adequate ventilation during anesthesia. The most important factor for accomplishing this is a free airway. When there is any question of difficulty in maintaining an adequate supply of oxygen, an intratracheal tube should be inserted after induction of anesthesia. Kloty pointed out that obstruction of the upper or lower portions of the respiratory tract which prevents the free passage of air to the blood and tissues is always serious; he also emphasized the great importance of terminal blockage of large numbers of air sacs, which reduces vital capacity and interferes with adequate exchange of oxygen and carbon dioxide, as well as that of anesthetic gases. One of the greatest hazards of deficiency of oxygen, as demonstrated by Courville (6, 12), is its damaging effect on the central nervous system, particularly on the cerebral cortex. A few minutes of severe anoxemia may produce permanent damage. Waters (44) stressed the necessity of maintaining the integrity of the patient's mechanism for transportation of oxygen, of maintaining a free airway and maintaining adequate tidal exchange, by mechanical means if necessary. For the relief of pain, he further stressed caution in the use of drugs which may

aggravate respiratory depression and predispose to postoperative pulmonary complications (43). Asthma usually does not produce an untoward surgical risk. After both ether and intravenous pentothal sodium anesthesia, periods of relief from the asthmatic attacks have been observed.

Anemia frequently accompanies pathological lesions of the respiratory system and is present often when the patient is debilitated and when the risk of operation and anesthesia is great. This condition, owing to the lowered oxygen carrying capacity of the blood, interferes with adequate transportation of oxygen to the tissues. When concentration of hemoglobin is less than 8 to 10 grams per 100 cubic centimeters of whole blood, it is wise to give a blood transfusion before operation.

When indicated, the value of suction aspiration of the tracheobronchial tree during the immediate postoperative period is assuming major importance in relation to the control and prevention of postoperative pulmonary complications, such as atelectasis, massive collapse of the lung and bronchopneumonia (18, 30). According to Hinshaw, defective pulmonary drainage appears to be the primary cause of many cases of pneumonia after operation. If permitted to exist for long, depression of respiration during anesthesia and the formation of viscid mucus may plug a bronchus and lead to lobular, lobar, or massive collapse of the lung. The use of suction bronchoscopy is one of the greatest advances in helping to lower the incidence of postoperative pulmonary complications after anesthesia.

The administration of oxygen, whether by tent, nasal catheter, or special masks, such as the B.L.B. (Boothby, Lovelace and Bulbulian) oxygen mask, has become of routine importance in the postoperative management of surgical patients (8, 42). The administration of 100 per cent oxygen after operation has been useful in the relief of gaseous distention. Helium with mixtures of oxygen may be respired with less effort than oxygen or oxygen and air. Treatment with oxygen and helium has been beneficial after operation for patients who have asthma and mechanical obstruction to respiration as a result of infections, tumors, foreign bodies, or laryngeal edema.

DIABETES

Generally speaking, modern methods of diabetic therapy and anesthesia have lifted the diabetic patient out of the group of patients who present a poor risk. Unless these patients have other pathological conditions which in themselves would lead to abnormal hazards from surgical procedures and anesthesia, their outlook is generally favorable. Other conditions frequently do exist in cases of diabetes, among which are tendencies to coronary thrombosis and cerebrovascular accidents. Many clinicians are of the opinion that the diabetic patient under satisfactory control can even withstand the disturbance of such agents as ether without untoward reactions. This seems to be true, but with the anesthetic agents available we are of the opinion that we are justified in using those which interfere least with carbohydrate metabolism. Ether not only elevates the level of blood sugar but tends to produce acidosis as a result of postoperative vomiting and restriction of food. Nitrous oxide, ethylene, and cyclopropane are suitable since they only slightly affect carbohydrate metabolism. Anoxemia may result in acidosis and thus, cyclopropane is preferable to nitrous oxide or ethylene, unless these agents will produce adequate anesthesia without deficiency of oxygen. Neff and Stiles found that Bourne's buffer phosphate solution reduced the incidence of postanesthetic nausea and vomiting with cyclopropane anesthesia. Spinal and regional anesthesia also are satisfactory for diabetic patients. Pentothal sodium intravenously administered and used alone or in combination with local or regional anesthesia also is advocated. If it is necessary to operate on a patient who has uncontrolled diabetes, every effort should be made to control the diabetes before the operation is performed unless the operation is urgent. When stabilization has occurred, any of the suggested methods of anesthesia which are adequate for the operation may be employed and if ether is necessary, it may be used in minimal amounts.

AGENTS AND METHODS

It would be impractical to attempt to establish criteria for the types of patients who present poor surgical risks, but brief mention may be made of the potentialities of certain anesthetic agents. A discussion of chloroform and ethyl chloride is purposely omitted because of their toxicity. Divinyl ether and tribromethanol have a place in anesthesia, but the former is somewhat toxic to the liver, particularly for prolonged administration, and the latter produces toxic effect on both the liver and kidneys and is considered safe only when used as a basal anesthetic agent.

Nitrous oxide. On the basis of its low toxicity, nitrous oxide and oxygen is safe, but the toxic effect of the anoxemia which may accompany the anesthesia definitely is deleterious. If the nature of the operation will permit adequate oxygenation, the method is commendable in cases in which

risk is poor. Local or regional anesthesia used with nitrous oxide and oxygen permits larger interventions and is relatively safe for these patients.

Ethylene. Like nitrous oxide, the toxicity of ethylene is low and better oxygenation may be obtained than with nitrous oxide. Its uses parallel those of nitrous oxide.

Ether. Valuable as ether is in anesthetic practice, its use should be avoided as much as possible in cases of poor surgical risk, owing to its irritating action on the respiratory tract which predisposes to postoperative pulmonary complications, and the vomiting, acidosis, and hepatic dysfunction it causes.

Cyclopropane. The value of cyclopropane in many types of cases of poor surgical risk is incontestable on the basis of its low toxic effect on the liver and kidneys, its anesthetic potency with high concentrations of oxygen and absence of irritation to the respiratory system (45). Its use is particularly indicated in thoracic surgery (35).

Cyclopropane has certain disadvantages, however. It is a very potent gas and in high concentrations is thought to be toxic to cardiac muscle. Cardiac arrhythmias have been observed during the course of cyclopropane anesthesia, but ventricular fibrillation and complete heart block are among the few that are of grave significance. If local or regional anesthesia is to be used with cyclopropane, epinephrine is withheld from the local anesthetic solution since it increases the tendency to ventricular fibrillation (4, 10). Guedel suggested the combination of cyclopropane anesthesia with subarachnoid, peridural, or local block to increase abdominal relaxation in certain cases. Another hazard of cyclopropane anesthesia which cannot be overlooked is its explosiveness in anesthetic concentrations. It should never be used in the presence of cautery or other electrical apparatus. Steps are now being taken to decrease the hazard of electrostatic sparks, among which is intercoupling of the anesthetist, gas machine, patient, and operating table (20). When cyclopropane is used with all proper precautions, its advantages in certain cases of unfavorable risk far outweigh its hazards.

Intratracheal anesthesia. Respiratory obstruction and resultant anoxemia should never be allowed to persist when such difficulties may be promptly controlled by passage of an intratracheal tube. In cases of graver risk or in those in which complications are anticipated, its routine use may be advisable. The effortless breathing that results, the ease and control of anesthetic administration and oxygenation, and the facility of aspirating mucus through the tube, all favor better control. The intratracheal tube has another important use in addition to its use in anesthesia, that is, its value in resuscitation. Prompt resuscitative measures during operations in the presence of poor risk are required frequently. The effectiveness of treatment with oxygen and artificial respiration depends on the patency of the airway. The intratracheal tube assures a patent airway. Reid and Brace drew attention to the danger of altered cardiac and respiratory function and circulatory derangement as a result of irritation of the respiratory tract, particularly when anesthesia is light. This occurs as a result of reflex action in the autonomic nervous system by introduction of intratracheal tubes or other mechanical airways.

Local and regional anesthesia. Since procaine is the least toxic of local anesthetic agents, its use is preferred in the cases in which the risk of operation is great. Infiltration and block anesthesia, either alone or supplemented, continues to be one of the safest methods for such patients (26). In cases in which cardiac disease or hypertension is present, epinephrine is contraindicated in the anesthetic solution. Hypersensitivity to local anesthetic agents in certain cases must be borne in mind, as well as the inadvertent injection of the solution into a blood vessel.

A few regional methods may be mentioned. Cervical block, skillfully performed, produces adequate and safe anesthesia for most operations about the neck. For operative procedures on the upper portion of the abdomen, abdominal wall block, bilateral intercostal nerve block of the seventh to eleventh intercostal nerves, inclusive, and splanchnic block are valuable procedures. Splanchnic block, supplemented by one of the gases, in addition to either abdominal or intercostal block often is used for operations on the upper portion of the abdomen in cases in which the condition of the patient is unfavorable. Peridural block also may be used with relative safety. For operations on the anus, lower portion of the rectum, perineum, and prostate gland, sacral block carries a relatively wide margin of safety. Individual nerve block and simple infiltration frequently are adequate procedures for small interventions.

Spinal anesthesia. Spinal anesthesia, although preferred in certain cases of poor operative risk often is contraindicated in others. Here again, procaine is the agent of choice, but if the risk of operation for the patient is fair the use of metycaine may be considered because of the longer duration of effect.

Regardless of other factors, spinal anesthesia is contraindicated when the value for hemoglobin is less than 50 per cent (Dare), or persistent hypotension, disease of the central nervous system, or marked debility exists. Spinal anesthesia is the preferred method for many acute abdominal conditions and for operations in the presence of intestinal obstruction. Spinal anesthesia is safer for operations on the lower portion of the abdomen than on the upper. In considering spinal anesthesia for a patient of doubtful risk, it must be remembered that varying degrees of circulatory and respiratory deficiency are produced through paralysis of the sympathetic and intercostal nerves. These conditions increase in severity with the height of the spinal anesthesia, and this circulatory and respiratory deficiency leads to deficiency of oxygen and varying degrees of anoxemia, the dangers of which have been pointed out.

The method of continuous spinal anesthesia as advocated by Lemmon (*22*, *23*) has certain advantages for prolonged operations in which spinal anesthesia appears to be the method of choice. Its use may be advantageous for spinal anesthesia for certain patients whose condition is unfavorable and for whom it is not desirable to give a dose of the spinal anesthetic agent sufficient for the whole operation. By using the continuous method, a minimal dose is administered and if the patient is reacting favorably to the effects of the spinal anesthetic, subsequent doses may be added as required. In this way it may be possible to prevent circulatory and respiratory insufficiency, which often occurs after a single large dose of a spinal anesthetic agent has been given.

Intravenous anesthesia. Pentothal sodium is the anesthetic agent of choice in intravenous anesthesia. Evipal soluble (sodium salt of n-methyl-C-C-cyclo-hexamyl-methyl barbituric acid) although less potent, also is short acting and satisfactory. In cases in which intensive treatment with sulfanilamide has been given up to the time of operation, evipal soluble is preferred since it does not contain sulfur. Adriani (*2*) demonstrated that evidences of increased toxicity occur when pentothal sodium is administered to animals that have been receiving sulfanilamide. Lorhan and his associates concluded from their experiments that no cumulative toxic action on the liver or kidneys occurred from the administration of sulfanilamide and evipal soluble. It is generally felt that the concurrent use of these agents should be with caution, if at all.

Ordinary anesthetic doses of pentothal sodium have relatively little effect on the liver and kidneys, but when the drug is administered too rapidly or in too large doses respiratory function is depressed acutely. A 2.5 per cent concentration is preferred. The normal heart and the heart in which reserve is within normal limits tolerate the effects of pentothal sodium well. Advanced myocardial degeneration associated with dyspnea is a definite contraindication to its use. Most patients, even when debilitated and intoxicated, tolerate the effects of intravenous anesthesia satisfactorily, provided anoxemia is prevented. The risk to the patient is increased when, in order to produce satisfactory relaxation for certain operations, marked respiratory depression and anoxemia are allowed to persist.

The recent trend of opinion is pointing more and more to the increased usefulness and safety of intravenous anesthesia combined with various other methods.

Comment. If it is possible to generalize concerning anesthesia in cases of grave surgical risk, it may be said that combinations of regional anesthesia and cyclopropane and oxygen anesthesia, or regional anesthesia, intravenous anesthesia and nitrous oxide and oxygen anesthesia possess the widest margin of safety. The latter combination obviates the hazard of explosion or fire. Abdominal wall and intercostal block, when supplemented by intravenous anesthesia and the continuous administration of oxygen or 50 per cent nitrous oxide and 50 per cent oxygen by inhalation, is one of the safest methods for anesthetizing patients of doubtful risk. Light pentothal sodium anesthesia forms a satisfactory supplement to spinal anesthesia when indicated and aids in the control of nausea and mental trauma. Small doses, slowly administered, are indicated, since the circulatory and respiratory functions already are depressed by the spinal anesthesia.

RISK AND THE OPERATIVE PROCEDURE

Certain operations carry with them more than the usual degree of risk. Anticipation of the added risk of such procedures to that already existing is necessary from the standpoint of intelligent supportive therapy during the operation. Intracranial interventions usually are serious. It is important that the method of anesthesia does not elevate intracranial pressure. Open drop ether administered by means of an intratracheal tube is satisfactory for many intracranial operations, since an obstructed airway tends to elevate intracranial pressure.

Operations on the thyroid gland do not carry the risk they did in the past, owing to the preoperative management of the patient. Crile (*14*) stated that the only two absolute contraindica-

tions to operation on the thyroid gland are persistent delirium and persistent vomiting. Local infiltration in addition to gas and oxygen anesthesia usually is satisfactory. In cases in which the gland is exceptionally large or is substernal, tracheal collapse because of prolonged pressure on the trachea is a serious potential complication. In such cases, intratracheal anesthesia is the safest method, or at least, facilities for prompt intratracheal intubation should be available. Patients who do not respond favorably to preoperative medical treatment present more serious risks than those whose basal metabolic rate and pulse rate do drop satisfactorily after medical treatment. When the basal metabolic rate and pulse rate continue to remain above normal levels despite treatment, many surgeons prefer to perform thyroidectomy in two stages.

Most intrathoracic operations, such as lobectomy, pneumonectomy, and open drainage for emphysema, carry unusual risk. All open operations on the thorax require delicate anesthetic control, owing to disturbances of respiratory function. Cyclopropane administered by means of an intratracheal tube permits better anesthetic control than any other method. This method often is chosen for operations on the diaphragm, such as in repair of diaphragmatic hernia. Slight amounts of ether sometimes may be added to increase the degree of relaxation and exposure.

Operations on the stomach, duodenum, gall bladder, liver, and spleen may present serious anesthetic problems.

Either low spinal anesthesia or intravenous anesthesia with pentothal sodium as the anesthetic agent has been the preferred method for transurethral prostatic resection or for other manipulations on the urethra or bladder (39). Many of these patients are in poor condition because of their advanced age, debility, and the prolonged retention of urine which has resulted in retention of nitrogenous waste products and uremia.

SUPPORTIVE MEASURES

Modern methods of preoperative and postoperative treatment and advances in the field of surgical shock and supportive therapy have changed the condition of many patients from that which constituted a poor surgical risk to one for which the risk was fair or even good. Modern methods of intravenous therapy, such as administration of sodium chloride, dextrose, and so forth, have been important. Coller and Maddock mentioned the importance of the kidneys in maintaining water balance. They stated that for seriously ill patients, particularly those who have a septic condition, severe disease of the biliary tract or some renal impairment from any cause, an intake of water that provides at least 1,500 cubic centimeters of urine daily is often desirable. Intravenous therapy is important in maintaining water and electrolyte balance, when, because of vomiting, fluids cannot be taken by mouth. Drew and associates stated that in the presence of shock, treatment, to be rational, must overcome the severe arteriolar and venular spasm, the capillary paralysis and dilatation and the great loss of circulating blood volume. Hypertonic solution of sodium chloride is used successfully in relieving these effects. The use and value of chemotherapy, particularly with the sulfonamide compounds, for infective conditions, is well known.

High in the scale of importance is the treatment of shock during and after surgical operations (40). Shock occurs during operation as a result of several factors, for instance, the anesthesia, operative manipulation and trauma, dehydration, hemorrhage, fear, exhaustion, and anoxemia. Shock, as Moon has pointed out, may become a vicious cycle, associated with low blood pressure, low volume of circulating blood, and hemoconcentration. This circulatory deficiency is associated intimately with oxygen want in the tissues and with atony of the capillaries. Shock, if allowed to persist without treatment, tends to become irreversible. Varying degrees of shock occur during any operative procedure, depending on the preoperative condition of the patient, the anesthetic, and the type and duration of the operation. It is obvious that debilitated, anemic, toxemic, and functionally abnormal patients will succumb to shock both more easily and to a more profound degree than will more normal patients. Therefore, the anticipation of the need of treatment for shock is particularly important in a case in which the risk of operation is poor.

If shock is to be treated effectively, it must be treated promptly. Better still, if it is known that the patient is in poor condition, the shock should be treated before it actually occurs. This is accomplished by various measures, depending on the urgency. A fall in blood pressure during the operation need not be serious if it is not persistent and if it is not associated with marked loss of fluid or blood. Vasopressor agents, such as ephedrine or neosynephrin hydrochloride, may be injected intramuscularly or intravenously in order to elevate the blood pressure. If the fall in blood pressure occurs in the presence of marked loss of fluid (profuse sweating) or is obviously attributable to hemorrhage, vasopressor agents give only transient relief and a false sense of security.

A pale, cold, clammy patient is in a state of shock and needs fluids, blood, or both. In the management of patients for whom the risk of operation is great it is safest to start an infusion of physiological saline solution or a 5 per cent solution of dextrose in physiological saline solution at the beginning of the operation. In this way it is possible to combat dehydration and shock during the operation by compensating for loss of fluid and maintaining the volume of circulating fluid and the electrolyte balance of the tissues. In addition, if shock appears suddenly or if any emergency, such as profuse hemorrhage, occurs, there is no delay in the administration of fluids or blood. Loss of minutes in the institution of treatment for shock may cost the patient his life, particularly if he is in poor condition. Transfusion of blood is the best means of combating shock. The amount necessary will depend on the preoperative level of hemoglobin, the amount of blood lost during the operation, and the response of the blood pressure, pulse rate, blood volume, color, and skin. Refrigerated blood from universal donors has simplified prompt treatment. If blood is not readily available, administration of fluids may be followed by administration of a 6 per cent solution of acacia until blood can be obtained. The use of plasma, which can be stored in the desiccated state and redissolved before use, provides all the elements of whole blood for treating shock, with the exception of erythrocytes. By its use, shock may be controlled for several hours, even after marked hemorrhage has occurred.

SUMMARY

Anesthesia in relation to pathological conditions which go to make up the so called poor risk has been discussed, and suggestions made as to choice of anesthetic agents and methods.

Stress has been laid on the value of certain types of treatment and supportive measures which help to favor the operative and postoperative outlook and lessen the degree of risk.

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STUDIES OF THE ANALEPTICS: II. METRAZOL

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In a previous paper (27), we have reported experiments dealing with the antagonistic action of coramine (nikethamide) against ether and chloroform. In this paper we present an analogous series of experiments designed to make a similar determination of the antidotal value of metrazol or pentamethylenetetrazol against overdoses of ether, divinyl ether, and chloroform.

Metrazol has the distinction of acceptance by the Council on Pharmacy and Chemistry of the American Medical Association. Although closely related to camphor in its pharmacological and therapeutic applications, metrazol has a more rapid and intense action due, probably, to its greater solubility in the body fluids. The voluminous literature dealing with metrazol up to 1937 is reviewed by Hildebrandt (12).

A definite antagonism has been shown to exist between metrazol and certain members of the hypnotic group, particularly the barbiturates. Thus, Tartler and later Maloney found metrazol an efficient antagonist to sodium barbital in rats. Werner and Tatum and also Barlow have reported that metrazol is an efficient antagonist to pentobarbital in rabbits.

Several investigators including Hildebrandt (11), Helaeirs, and later Lendle found that metrazol increased the respiratory rate and volume in morphine depressed rabbits. An awakening action has been observed against small doses of avertin by Barlow but he found that metrazol was not lifesaving in the presence of fatal doses of avertin. Schoen has reported that the depression produced by ethyl alcohol in rabbits is considerably reduced by metrazol but, according to McCrea and Taylor, this antagonism is demonstrable in dogs only when the dose of alcohol is sublethal. In their experience, lethal doses of alcohol are not successfully combated even by very large doses of metrazol.

Apparently the antidotal efficiency of metrazol, as is the case with coramine (27), varies with the depressant. Thus, Axmacher, as well as Maloney and Tatum, found that there was little antagonism between urethane and metrazol in rabbits. Similarly Whitehead and Draper (26) obtained no evidence of a diminution of chloralose or urethane depression in dogs and cats.

Although metrazol is widely employed by clinicians to treat emergencies developing under the inhalation anesthetics, there are few controlled experimental studies which support this use. Some experimenters have found it of no value. Thus Camp (4) found that metrazol exerted little or no action on the respiratory center of rabbits and dogs deeply depressed by ether and chloroform. Similar results are reported by Jackson. In deeply etherized dogs, Jackson found that metrazol produced tremors or convulsions with little or no stimulation of the respiration. Evipal depressed dogs, on the contrary, responded to metrazol with marked specific respiratory stimulation and no tremors or convulsions.

It appears, therefore, that the use of metrazol against the barbiturates and certain of the other depressants is supported by a considerable body of experimental evidence. The experimental basis for the use of metrazol in emergencies occurring under inhalation anesthesia is less convincing.

TECHNIQUE

Measured per kilogram doses of ether, divinyl ether, and chloroform were administered to healthy mongrel dogs by the same method which we employed in our coramine experiments. This method is more fully described in a previous paper (5). In brief, the apparatus is a closed soda lime absorption system having a capacity of approximately 5.5 liters, within which the anesthetic is volatilized in an atmosphere of pure oxygen. The mask contains a rubber diaphragm through which, by means of a syringe and needle, the dose of the anesthetic is injected on to a wire screen for volatilization. The mask is fitted tightly to the dog's muzzle by means of a rubber face piece. Every effort was made to prevent gas leakage at this point and the entire system was checked frequently for leaks. Volatilization of the anesthetic within such an apparatus is rapidly completed, and the drug develops its maximum effects within an average period of 2 minutes. The experiments were performed at intervals of 4 days.

The minimal dose of each of the three anesthetics required to produce an apparently per-

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manent respiratory arrest was established for each animal by repeated experiments. For this purpose the initial dose employed was below the average of the series. It was then increased or decreased as required until we had determined the amount of the drug which produced an apparently permanent respiratory arrest in not less than 2 of 3 consecutive experiments and which, when reduced by 10 per cent produced arrest in not more than 1 of 3 consecutive experiments. When the respiratory paralysis had lasted 10 to 15 seconds the mask was removed and the animal was resuscitated by artificial respiration and the administration of oxygen. An essential feature of this technique is that the dose required for each animal is repeatedly confirmed—a procedure which helps to eliminate technical errors. After the minimal dose for respiratory arrest, as here defined, had been determined for each individual dog, a second series of 3 anesthesias was administered, each consisting of this predetermined dose. As soon as the animal had passed into deep surgical anesthesia but before the appearance of respiratory arrest, 0.05 cubic centimeters per kilogram of a 10 per cent solution of metrazol was injected intravenously—a dose of metrazol equivalent for the average adult human to 3.5 cubic centimeters of the commercial 10 per cent solution. In the event of respiratory arrest the animal was resuscitated by the same method used for the controls. There was no indication that tolerance to the anesthetics developed in the course of these experiments (5).

EVALUATION OF AN ANALEPTIC

The first step in the evaluation of an analeptic should be an accurate assay of the quantitative toxicity of the depressant. With this information as a basis it is possible to balance the antidotal action of the analeptic against a standardized depth of depression. Unless the experiments are carried out in this orderly manner the resulting data become so haphazard that the relative efficiency of the various analeptics cannot be ascertained. This is the confused situation now obtaining with respect to the relative value of the numerous drugs recommended for use in emergencies developing under inhalation anesthesia. Consequently, in this attempt to study the analeptics, our first concern has been with the development of an accurate method for the determination of the quantitative toxicity of ether, divinyl ether, and chloroform.

The best evidence for the reliability of a method of bio-assay is the ability of the user to obtain consistent median doses for the production of a standardized pharmacological effect. The data presented in Table I show that the technique we have devised has yielded consistent median doses for respiratory arrest in three successive series of animals. The doses given refer to cubic centimeters of the anesthetic per kilogram of dog.

TABLE I.—CORRESPONDENCE OF MEDIAN MINIMAL DOSES FOR RESPIRATORY ARREST

Series*	Ether	Divinyl ether	Chloroform
A	1.65	0.70	0.175
B	1.75	....	0.185
C	1.69	0.66	0.180

*The number of dogs in each of the series was as follows: Series A—ether 35, divinyl ether 35, chloroform 35; Series B—ether 10, chloroform 19; Series C—ether 16, divinyl ether 19, chloroform 17.

EXPERIMENTAL RESULTS

1. Influence of metrazol upon the minimal dose required to produce respiratory arrest. The influence of an injection of metrazol upon the development of respiratory arrest following the administration of the individually determined minimal dose for respiratory arrest of the three anesthetics is shown in Table II. Data from a previous paper dealing with coramine (27) were incorporated in the table in order to facilitate a comparison of the antidotal efficiency of these two drugs.

It is apparent that metrazol, under the experimental conditions employed, is capable of significantly reducing the percentage of respiratory arrests from the minimal dose for respiratory arrest of ether and divinyl ether. Its antidotal value, however, should not be exaggerated because a much greater reduction in the incidence of respiratory arrest can be obtained if the dose of the anesthetic is reduced by only 10 per cent. The important implication of this fact for resuscitation is discussed in the next paragraphs. The percentage of respiratory arrests from the minimal doses for respiratory arrest of chloroform was not significantly reduced by metrazol. Evidently the respiratory effects of chloroform are more difficult to combat than those of ether and divinyl ether. In the case of all three anesthetics visible stimulation of respiration only occasionally followed injection of the drug. It is noteworthy that coramine completely failed to reduce the incidence of respiratory arrest from both ether and chloroform.

2. The influence of metrazol upon the probability of resuscitation. Resuscitation from respiratory arrest produced by an inhalation anesthetic is a race between the elimination of the toxic agent

TABLE II.—INFLUENCE OF CORAMINE AND METRAZOL UPON THE AMOUNT OF ETHER, DIVINYL ETHER, AND CHLOROFORM REQUIRED TO PRODUCE RESPIRATORY ARREST

Ether	No. of dogs used	Total administrations of minimal dose for respiratory arrest	Percentage of administrations resulting in arrest
*M.D.R.A. alone	26	114	80
M.D.R.A. plus coramine	10	28	75
M.D.R.A. plus metrazol	16	48	52
M.D.R.A. reduced by 10 per cent	26	54	22
Divinyl ether			
M.D.R.A. alone	19	43	93
M.D.R.A. plus metrazol	19	57	53
M.D.R.A. reduced by 10 per cent	19	46	17
Chloroform			
M.D.R.A. alone	36	109	86
M.D.R.A. plus coramine	19	64	90
M.D.R.A. plus metrazol	17	51	73
M.D.R.A. reduced by 10 per cent	36	82	22

*The M.D.R.A. is the Minimal Dose required to produce Respiratory Arrest in at least 2 of 3 consecutive administrations.

through the lungs and the development of its fatal effects upon the circulation. A drug can be properly termed analeptic only if its use helps to win this race. The definitive test for analeptic action, therefore, should determine the influence of the drug upon the probability of resuscitation. So far as we are aware, no other controlled studies of analeptics have been made which subject them to this critical test against otherwise fatal doses of the inhalation anesthetics.

In the course of the experiments here reported we have carried out 542 resuscitations from respiratory arrest produced by overdoses of ether, divinyl ether, and chloroform both with and without the aid of analeptics. This has given us the opportunity to determine the influence of metrazol and of coramine upon the probability of resuscitation. All our resuscitations have been conducted under conditions controlled so as to make them identical with the exception of the anesthetic and the analeptic employed. The data are presented in Table III.

TABLE III.—INFLUENCE OF CORAMINE AND METRAZOL UPON THE PROBABILITY OF RESUSCITATION

Ether	No. of dogs used	Respiratory arrests produced	Failures to resuscitate	Percentage failure to resuscitate
Control resuscitations	28	149	2	1.4
Resuscitations with coramine	10	21	0	0.0
Resuscitations with metrazol	16	25	0	0.0
Divinyl ether				
Control resuscitations	26	81	3	3.7
Resuscitations with metrazol	19	30	0	0.0
Chloroform				
Control resuscitations	53	154	15	9.7
Resuscitations with coramine	19	45	5	11.0
Resuscitations with metrazol	17	37	0	0.0

Of the 149 control attempts at resuscitation from an overdose of ether only 2 or 1.4 per cent resulted in failure. The relatively low probability of failure to resuscitate when ether is the anesthetic makes it difficult to determine the value of a pharmacological antidote but, as will be noted, there were no failures to resuscitate following the administration of either coramine or metrazol. It is quite possible that the absence of failures to resuscitate in the ether experiments was due to the smallness of the analeptic series.

The probability of failure to resuscitate was somewhat greater in the divinyl ether series. In the 81 control attempts to resuscitate, 3, or 3.7 per cent, were unsuccessful but again there were no failures to resuscitate in the 30 respiratory arrests treated by an injection of metrazol. The probability of failure to resuscitate from an overdose of divinyl ether in the control experiments was not sufficiently high to warrant the conclusion that metrazol was an aid to resuscitation.

The much higher mortality resulting from an overdose of chloroform affords a better opportunity for the evaluation of an aid to resuscitation. In 154 control attempts to resuscitate, 15, or 9.7 per cent, ended in failure. Following the administration of coramine, there were 5, or 11 per cent, failures to resuscitate in 45 attempts. It is apparent that the addition of coramine did not increase the effectiveness of artificial respiration and oxygen. On the other hand, we experienced no failures to resuscitate in the 37 experiments in

which metrazol was injected. The conclusion seems warranted that metrazol increased the probability of resuscitation from a standardized dose of chloroform.

EVALUATION OF STUDY

The varied and complicated circumstances surrounding death under anesthesia always provide a plausible explanation for the tragedy but, in the final analysis, the same ultimate cause must be assigned—there has been a failure to resuscitate. Resuscitation, therefore, is the master key to safety in anesthesia.

It is something of a paradox that much of the greater safety of ether is due to the fact that it causes respiratory paralysis earlier in the course of the poisoning than is the case with chloroform. Ordinarily in ether anesthesia the respiration ceases—that is to say, a further amount of the poison is rejected—while the circulation is still in comparatively good condition. Under these circumstances there is a greater probability of resuscitation than would be the case if, through postponement of respiratory failure, the subject inhaled a concentration of ether more injurious to the circulation. Thus early respiratory arrest may be regarded as an automatic safety mechanism which operates to limit the intake of an inhalation anesthetic to the minimal respiratory arresting dose. No such mechanism, of course, exists to protect the circulation from a fatal overdose of a nonvolatile anesthetic.

The period of time separating respiratory arrest from circulatory failure might be termed appropriately "the resuscitation interval" because it is only during this interval that attempts at resuscitation are likely to be successful. One of the most important factors operating to determine the probability of resuscitation, therefore, is the length of the resuscitation interval. It is possible, under certain circumstances, for the administration of a respiratory stimulant to shorten this interval by postponing respiratory arrest and in this way actually to diminish the probability of resuscitation unless the drug simultaneously increases the resistance of the circulation to the anesthetic. Some so called analeptics are, at least potentially, injurious to the circulation. There is reason to believe that this may be the situation with respect to alpha-lobeline (Camp, 3; Whitehead and Elliott) and coramine (Peters and Visscher).

Our own unpublished experience with lactic acid is a further illustration of this point. Lactic acid powerfully stimulates the respiration and is capable of delaying respiratory arrest from chloroform but it is also injurious to the circulation. Consequently, it acts to shorten the resuscitation interval at both ends: first by delaying respiratory arrest and second, by hastening circulatory failure. Although its administration results in some reduction in the incidence of respiratory arrest from a standardized dose of chloroform, any such advantage is more than overcome by the reduced probability of resuscitation, should respiratory arrest develop. Our experience with lactic acid and other respiratory stimulants has impressed us with the view that it is the behavior of the circulation which determines the final outcome of an attempt to resuscitate and that respiratory arrest, at least when produced by the inhalation anesthetics, should be treated with analeptics chosen for their circulatory rather than their respiratory effects.

The reasons for our position can be made clearer by a brief consideration of the physiology of resuscitation. In the great majority of instances respiratory arrest occurs before the concentration of the anesthetic becomes sufficient to cause failure of the circulation. Although, absorption of the poison does not continue after respiratory arrest there is, unfortunately, a rapid development of anoxemia. The ultimate failure of the circulation is the result of disastrous synergism between anoxemia and the anesthetic. Forced ventilation of the lungs following respiratory arrest merely replenishes the oxygen supply within the lung alveoli and removes the anesthetic from these passages. This alone will not ensure resuscitation. For success the circulatory minute volume must be large enough to provide effective transport of these gases between the lungs and the body tissues. The most efficient artificial respiration cannot save a patient whose circulation lacks the necessary vigor.

We have shown in Table II that the removal of a small amount of the anesthetic will act more effectively to restore spontaneous respiration than will the injection of a respiratory stimulant. Moreover, the highly developed mechanical methods now available for forcible ventilation of the lungs greatly reduce our dependence upon pharmacological respiratory stimulants. However, the position is otherwise if the analeptic acts upon the circulation to speed the rate of transport of gases between the lungs and tissues. Such a drug should be a very useful aid to resuscitation.

In this connection it is of interest that an increased cardiac minute output after metrazol was observed in animals by Mueller, and by Gollwitzer-Meier and also in humans by Groscurth and Bansi and by Hoen and Neuthard. Doses of

the order we have used in our experiments have been shown by Haury and Gruber to dilate the peripheral vessels. A favorable action upon the circulation depressed by chloroform has been observed by several workers including Eichler and Hildebrandt, Russu and Spârchez, and Leffkowitz.

There is thus some experimental support for the view that metrazol may aid resuscitation from chloroform overdose through a stimulant action upon the circulation which tends to lengthen the resuscitation interval and to increase the rate of gas transport between the lungs and tissues.

SUMMARY AND CONCLUSIONS

1. Metrazol increases slightly the amount of ether and divinyl ether but not of chloroform required to produce respiratory arrest in dogs. Only occasional brief stimulation of the respiration is seen when metrazol is injected in toxic anesthesia produced by these agents.

2. In 542 attempts to resuscitate from respiratory arrest produced by ether, divinyl ether, and chloroform were carried out by means of artificial respiration and the administration of oxygen with and without an injection of metrazol or coramine.

3. Of 149 attempts to resuscitate from ether overdose without the aid of an analeptic 2, or 1.4 per cent, were unsuccessful. In 81 similar control resuscitations following an overdose of divinyl ether 3, or 3.7 per cent, ended in failure. The mortality from an overdose of chloroform was much higher and attempted resuscitation failed in 15, or 9.7 per cent, of the 154 control experiments. There were no failures to resuscitate when metrazol was administered in addition to artificial respiration and oxygen in the treatment of 25, 30, and 37 respiratory arrests produced by ether, divinyl ether, and chloroform, respectively.

4. The low probability of failure to resuscitate without the aid of an analeptic from an overdose of divinyl ether and especially from ether makes evaluation of a pharmacological aid to resuscitation difficult. When the very high incidence of failures to resuscitate from chloroform induced respiratory arrest in the control series is contrasted with the complete absence of failures when metrazol was administered, the conclusion seems justified that metrazol was useful as an aid to resuscitation.

5. As previously reported, coramine does not exert a favorable influence upon the probability of resuscitation from an overdose of chloroform.

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EDITORIALS

SURGERY
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MAY, 1942

EXTENSION OF INDICATIONS FOR RADICAL OPERATION IN CANCER OF THE RECTUM

SIR W. ERNEST MILES made a noteworthy contribution to the surgery of cancer of the rectum when he emphasized the possibility of lateral and high lymphatic involvement in the disease and in 1907 strongly recommended the one stage abdominoperineal operation as the one which insured the greatest guarantee of complete removal of the carcinoma and its local extensions. In the Lettsomian lectures which he delivered in 1923 he traced the development of the surgical treatment of carcinoma of the rectum from the purely local operations to the much more radical one stage abdominoperineal operation and made a report of 116 such operations which he had performed. Radical operations were carried out in only 29.3 per cent of the patients coming under his care. Of his first 63 one stage resections there was a 36.2 per cent mortality rate and no patient over sixty survived. In the next 53 operations his mortality fell to 9.3 per cent, which he modestly attributed to the use of better anesthesia. Patients over sixty-five years of age, fat patients, patients with arteriosclerosis, diabetes, tuberculosis, Bright's disease, were considered unsuitable for operation. Growths attached to surrounding soft parts were not considered amenable to operation.

Since that time Miles' advocacy of the one stage abdominoperineal operation has been accepted as the operation of choice in many clinics and additional knowledge of the frequency of carcinomatous involvement of the lymphatic glands (65 per cent in removed specimens) as well as the height of their involvement has tended to confirm the soundness of that choice. Extension of the indications for operation has also increased in the last five years due to the maintenance of a relatively low operative mortality rate and increased knowledge as to what can be done surgically to carefully prepared patients. The extension of indications for resection of carcinoma of the rectum has been also furthered by the radioresistant character of cancer in this region, which leaves surgery as the outstanding chance for cure of these patients according to our present knowledge.

As Gilchrist and I have recently reviewed our last ten years' experience in the selection of patients with cancer of the rectum for radical operation, I was asked to comment on our findings in this editorial. The material studied concerned 277 patients coming to our service in the Presbyterian Hospital for operation. Five were considered inoperable. Two hundred seventy-two patients were operated upon and 179 had a radical removal

of the tumor with a hospital mortality of 7.2 per cent and a resectability rate of 65.5 per cent. Ninety-three patients were found to be unsuited for radical removal of the tumor due to extensive liver metastasis in 40, infiltration of the growth into the base of the bladder in 28, and marked infiltration of the growth into the prostate, vagina, or sacrum in 25.

Of the 179 patients from whom the tumor was removed, 105 presented some doubtful factors concerning the possibility of completely removing the tumor or in making the operation more difficult than usual. These factors were in the main: age over sixty-five years, adiposity, one or two small suspicious nodules in the liver, obliterative pelvic peritonitis from previous pelvic operation or diverticulitis, attachment of the tumor to the bladder, abdominal wall, adnexa, prostate, ureter, urethra, vagina or sacrum, and constitutional disease as diabetes or heart disease. Of this group of 105 patients the operative mortality rate was 9.5 per cent. In 74 favorable cases where there were no doubtful factors the operative mortality rate was 4.3 per cent. The long term survival rate can not be given at this time but in general it can be said that there are many of these patients who came in the doubtful group who have lived three to five years.

The consideration of a few of the doubtful groups may emphasize the value of extension of the indications for radical operation in cancer of the rectum.

There were 38 patients over 65 years of age given the benefit of removal of the tumor with four deaths (pneumonia or embolism). Nine of these patients were operated upon more than five years ago and five are still alive.

One of the most difficult decisions to make in favor of radical removal of the tumor is in patients in whom the tumor is adherent to structures outside of the bowel. A large part of the prostate was removed with the tumor in 5 patients, the rectovaginal septum in 6, the uterus and adnexa in 4, the ureter in 2, the dome and posterior half of the bladder in 1, and another loop of bowel in 1 patient, with 2 deaths in all groups.

There were 16 patients who had one or two small nodules in the liver in whom it was difficult to be sure that the growths were carcinoma and in whom radical resections were done. Four of these patients died of cancer of the liver on an average of ten months after operation but four others are alive and well three to seven years after operation.

In very fat patients there is no doubt an added risk of hemorrhage, infection, evisceration, and cardiovascular accidents, but in view of the extremely poor prognosis in nonoperative treatment we did not consider adiposity a contraindication for operation. Of eleven very fat patients there was one death from embolism and one evisceration which was repaired successfully.

No more details of problem groups will be considered here, and it only remains to suggest that radical operation for cancer of the rectum can be carried out in an increasing number of patients and that it offers the patient the best chance of cure provided the preoperative treatment of decompression of the bowel and restoration of the blood to normal (cells, electrolites, vitamin content, sugar, chlorides, plasma protein) as well as safe anesthesia and a reasonable surgical technique are considered essential principles.

VERNON C. DAVID.

ANATOMY AND SURGERY OF DIAPHRAGMATIC HERNIA

DURING the past twenty-five years there has been a rapid and progressive increase of interest in diaphragmatic hernia, and it has become apparent

that the condition is far more common than had been realized. It is curious that during this period of awakened interest in anatomical defects in the diaphragm, there has been no corresponding revival of curiosity about its origin and structure. As a matter of fact, most English textbooks of anatomy and embryology have either made no changes in their discussions of this subject or have curtailed them so much in the latest editions that they leave much to be desired in both clarity and completeness. This state of affairs is remarkable in view of the fact that Ballon has shown, in a recent historical review, that the diaphragm has fascinated anatomists for centuries. Perhaps anatomy has become too completely divorced from surgery.

The diaphragm is something of an afterthought in the evolutionary process, being present as a complete septum only in mammals. The major part of it is assembled from three ill assorted structures, the septum transversum (itself something of an embryological enigma), the pleuroperitoneal membranes, and the dorsal mesogastrium. These structures descend from the cephalic portion of the celomic cavity on different time schedules and finally unite to form a single complete septum between the abdominal and thoracic cavities at about the seventh or eighth week of fetal life. Obviously, any disturbance of the orderly progress of this intricate process may result in the formation of defects in the diaphragm.

The phrenic nerve develops and descends with the segment formed from the septum transversum and invades the remainder of the diaphragm after fusion of the three segments. If this invasion is arrested prematurely, the musculature of that part of the diaphragm that has not received a nerve supply probably undergoes atrophy, leaving only the peritoneum and the pleura to separate the two great body cavities in that particular location.

Soon after the diaphragm becomes a complete septum, the mid-portion of the celomic cavity is rapidly expanded by growth of the liver, and the resulting tension of the diaphragm causes it to pick up from the body wall a supplementary rim of tissue. One would therefore expect the diaphragm to be continuous with the inner layer of the abdominal cavity. Recent anatomical studies by D. D. Baker have shown that this is actually the case and that the conventional descriptions of the attachments of the diaphragm are incomplete and to some extent inaccurate. He finds that the anterior and lateral portions of the diaphragm are continuous with the transversus abdominis muscles and the posterior sheath of the rectus muscles. The attachment of these structures to the costal arch is by means of what is, in effect, a common aponeurosis. Likewise the posterior or lumbar segments of the diaphragm are continuous with the anterior layer of the lumbodorsal fascia, except for the central portion, which is attached to the bodies of the lumbar vertebrae.

While these observations are original with Baker, the idea is not new, for, according to Ballon, in 1676 Caspar Bartholin, son of Thomas, described the diaphragm and transversus abdominis muscles as a trigastric muscle, and in 1905 Sir Arthur Keith noted their developmental association.

A surgeon studying Baker's dissections is immediately struck by the fact that when the common aponeurosis of the transversus abdominis and the diaphragm is detached from the under surface of the costal arch, the diaphragm has been supplemented by a structurally similar fibromuscular membrane which increases its area by at least one-third. If there should be a very large defect in the anterior half of the diaphragm it could be closed without tension if the transversus abdominis were advanced into the thoracic cavity and

made to become a part of the diaphragm. Cadaveric dissections have shown that this procedure is entirely practical, although it has not as yet been employed in the living subject.

Large defects in the posterior half of the diaphragm cannot be closed by this method, but the principle of employing a flat fibromuscular sheet that, like the diaphragm itself, is continuous with the body wall, can be utilized. Using a posterior transthoracic approach we have bridged the hiatus in such a case with a flap developed from the latissimus dorsi, and have found that it served the purpose admirably. JAMES D. RIVES.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE title of the informal, chatty little book *Wounds and Fractures*[1] by H. Winnett Orr, may be misleading and prospective readers should be told that little space is devoted to the subject of wounds proper. Actually it is a treatise on fractures, in which stress is placed on the care of those associated with contaminated or infected wounds. As one might suspect from the name and fame of the author, wide open aseptic packing with vaseline gauze, coupled with rigid immobilization by the pin fixation plaster cast technique, is offered as the sine quo non of successful treatment in such cases. In this method Dr. Orr is, of course, a pioneer, and throughout the book the reader will find photographs, x-ray productions, and case abstracts covering every possible situation in which the method may be used.

Innumerable useful variations in technique are found, most of them simple and appealing to those working with barest essentials. The subject matter, the arrangement in which it is presented, and the distinction of the author combine to make this a valuable work. Let those who oppose the method for various well grounded reasons review the literature emanating from Europe during the past four years, and they will find that the method is becoming less and less controversial, certainly as it has to do with the wounds of war.

Solely as a textbook on fractures it probably is not suitable for students. It seems too advanced and broad enough view of the subject is not given. It should, however, be included in any collection of fracture texts. The principal lesson which the author intends to portray for the general practitioner particularly, is that the compound infected fracture, even with loss of substance, does not necessarily call for amputation.

J. K. STACK.

THE volume *Diseases of the Thyroid Gland*[2] "representing forty years of experience," dedicated to the author's grandchildren—"fellow students in medicine"—merely half a century behind him, is not intended as "a treatise on diseases of the thyroid gland" but as a "record of studies." It makes most entertaining reading and stimulating study. Anyone who makes iconoclastic assertions so persuasively and denies self-evident conclusions so forcefully is bound to stir up thought and this is certainly the main object of this book. The text is written in conversational style, which makes the reading so easy and rapid that before you know it you are taking something for granted which is certainly not the intention of the author. The thought-provoking character of the text may best be illustrated by a quotation: "Myxedema is a clinical term signifying a myxoid edema of the subcutaneous tissues. It is presumably due to lack of thyroid secretion. This opinion is based on the fact that the condition is ameliorated by giving thyroid extract. This represents about the sum total of our knowledge and has in a measure closed our eyes to some very obvious facts. It is first of all to be realized that the term myxedema is not synonymous with deficient thyroid secretion. This belief has been one of the sacred cows in medicine and any one who made merry with the old bossie did so at his peril, but the old critter has gone to the hamburger factory for ignominious extinction. It is important to keep this in mind because we know now that there can be a deficiency or an absence of thyroid secretion without any of the clinical signs of myxedema, as total thyroidectomies have abundantly shown. Nor is myxedema the superlative degree of thyroid dysfunction or the physical expression thereof. In cases in which myxedema is associated with a waning hyperthyroid state we have a combined minus and plus state. Our sacred bossie has become a hermaphrodite. This emphasizes the paucity of our fundamental knowledge." This paragraph reproduces the mixture so characteristic of the author's work, namely, of denial of much that has been scientifically demonstrated by others with violent assertion of personal knowledge certainly not shared by many students of thyroid physiology.

The volume contains 670 pages, is fully illustrated and well indexed, and will be enjoyed and valued by all interested in diseases of the thyroid.

PAUL STARR.

A COMPILATION of the experiences and an outline of the routine in the care of premature infants at the Sarah Morris Children's Hospital of the Michael Reese Hospital in Chicago are presented in *The Premature Infant*[3] by Hess and Lundeen. The great detail and step by step description of equipment and its use in the care of the premature infant should make this a good manual for any nurse interested in newborn or premature nursing setups. Although elementary in some respects it should be a valuable guide to any doctor in charge of a premature nursery. The chapters on asphyxia and oxygen

[1] WOUNDS AND FRACTURES; A CLINICAL GUIDE TO CIVIL AND MILITARY PRACTICE. By H. Winnett Orr, M.D., F.A.C.S. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1941.

[2] DISEASES OF THE THYROID GLAND; PRESENTING THE EXPERIENCE OF MORE THAN FORTY YEARS. By Arthur E. Hertzler, M.D. New York and London: Paul B. Hoeber, Inc., 1941.

[3] THE PREMATURE INFANT; ITS MEDICAL AND NURSING CARE. By Julius H. Hess, M.D., and Evelyn C. Lundeen, R.N. Philadelphia, Montreal, and London: J. B. Lippincott Co., 1941.

therapy, admittedly two of the most important subjects in premature care, are very brief. The subject of vitamins is given considerable discussion as are the care and management of a wet-nurse. A helpful description is given of the various diagnoses and treatment procedures, such as spinal puncture and the administration of intravenous fluids. Some of the major and minor disorders that occur in the premature infant are briefly described. This book is concluded with a rather interesting and enlightening chapter on the late mental and physical development of premature infants. L. MARTIN HARDY.

IN the Oxford War Manual[1] the author has briefly summarized the treatment of burns. Most of the English authors in the current literature are not in agreement with the tannic acid method as advocated in the volume, and there has been much added to the local treatment of burns since this volume was published.

The early chapters on classification and clinical course of burns are excellent. The method outlined for recognizing and combating burn shock and toxemia are practical and up to date.

In the complications of burns, chapter IV, the author ignores the subject of infection but later implies that infection is a normal sequel to all serious burns. This, in the reviewer's experience, is unjustified.

The greatest part of this volume is devoted to outlining in detail each step taken in the tannic acid method of treatment. He has only briefly mentioned the method of cleansing of the raw surface. This is in marked contrast to memorandum published later, E.M.S./Gen/343, circulated by the ministry of health for the guidance of medical officers which lays great stress on the proper method of cleansing the burned area with soap and water before the wound is treated by either open or closed methods.

The final chapter on the hospital care of burns simply outlines the various equipment needed but no mention is made of the scrupulous aseptic care which must be attained to prevent infection from occurring in these large open wounds.

With the exception of burn shock, too little of recent advances on this common war injury has been mentioned. HARVEY S. ALLEN.

TO correlate the clinical and pathological statistics relative to cancer of the face and mouth as found in a large clinic over a period of years is a tremendous task. In a clinic where cancer work has been carried on with an open mind as to the value of the various methods of treatment the summation of these findings should prove of immense value. Drs. Blair,[2] Moore, and Byars together with other members of their staff have presented their findings in view of the collective impression gained from the radiologist, the surgeon, and pathologist. They broaden the scope of the book by cementing the impressions of these combined groups rather than letting one "method" of treatment dominate.

The authors stress again and again that the doctor first seeing the patient is responsible for his ultimate fate. The convenience of certain methods of treatment used as a substitute for surgery does not remove the responsibilities from the shoulders of those first consulted by the patient.

The book must be read carefully to appreciate fully the authors' viewpoint, but the impressions gained are unmistakable and invaluable. Force is added to their contentions by numerous excellent photographs. A unique feature of the book is a large collection of line drawings under the heading of "Operative Technique" which shows graphically various steps in operative procedures, and these are in turn directly related to some particular case in the text.

A general impression of the scope of the book may be gained from a statement by Dr. Moore in which he says that the proper management of cancer means the proper co-ordination of surgery, x-ray and radium as a means of therapy. The use of any one "method" in all cases of cancer must be to the detriment of the patient.

This book should be of immense value to surgeons, radiologists, and dentists as well as the general practitioner, not only to tell them what to do but also to tell them what not to do. CLAIRE L. STRAITH.

AN attempt is made to summarize the knowledge of diseases of the heart and great vessels of the thorax in King's *Surgery of the Heart*.[3] Unfortunately, it has been given a title which does not accurately indicate its contents. While Dr. King has been primarily interested in surgical problems, the finished book has included almost all types of pathology which might affect the heart and the vessels immediately adjacent to it. A large number of conditions have been included which do not fall within the realm of "surgical diseases," nor could they conceivably be brought into this field at any future time. Indeed, the medical diseases are given more space in the book than are those which are being currently treated by the thoracic surgeon. Inasmuch as such a wide range of material has been collected here in book form, the volume would probably attain a wider range of usefulness for students and practitioners if it had been published under a more general title indicating its true scope. The author has probably intended that the cardiac surgeon should be familiar with all of the major lesions which might exist in the organ upon which he is operating; but in this attempt to set forth a broad view he has produced an imbalance so that the

[1] THE TREATMENT OF BURNS. By A. B. Wallace, M.B., F.R.C.S.Ed., M.Sc. (McGill). London: Humphrey Milford (Oxford University Press), 1941.

[2] CANCER OF THE FACE AND MOUTH; DIAGNOSIS, TREATMENT, SURGICAL REPAIR. By Vilray P. Blair, M.D., Sherwood Moore, M.D., and Louis T. Byars, M.D. St. Louis: The C. V. Mosby Co., 1941.

[3] SURGERY OF THE HEART. By E. S. J. King, M.D., M.S., D.Sc. (Melb.), F.R.C.S.(Eng.), F.R.A.C.S., Major A.A.M.C. Baltimore: Williams & Wilkins Co., 1941.

surgery of the heart has been pushed too much into the background.

The volume contains an admirable summary of the development of the heart, as well as its comparative anatomy. The normal anatomy is given at some length, but all too often the surgical implications of anatomical facts have been slighted or completely overlooked. Cardiac histology and physiology have been summarized. The chapter on radiological examination of the heart does not discuss angiocardiography. The treatise on electrocardiograms gives a good basic presentation of the normal types of graphs but it is deficient in consideration of abnormal forms.

While one might expect to find exhaustive descriptions and illustrations of surgical procedures in a book pertaining to this field, the volume is deficient in this regard. Of a total of 268 figures, only 9 are concerned with actual surgical technique or other therapeutic procedures, and all but one have been borrowed from the previous publications of other authors.

The reader is struck by the great lack of critical analysis of the results of therapeutic procedures, such as pericardiectomy for constrictive pericarditis, of total thyroidectomy for angina pectoris, of sympathectomy for angina pectoris, of surgical closure of the patent ductus arteriosus. Regarding alcohol injections of the sympathetic ganglia for angina pectoris, there is only a single sentence regarding postinjection alcoholic neuralgia. The impression is given that such a complication is rare. Unfortunately, this is not the true state of affairs as anyone who has had any appreciable experience with such treatments has found.

The author has covered the literature exhaustively; perhaps because of too great stress in this direction and because the author has included so little of his own personal experience in cardiac surgery the present volume lacks authority. Unfortunately, too, the book has been compiled at a time when surgical knowledge has been accumulating rapidly; hence the lag incurred by the process of publication has excluded from the volume several of the more recent advances in cardiac surgery which might be appropriately included in it. ROBERT E. GROSS.

THE form of *The 1941 Year Book of Radiology*[1] follows that established by its predecessors, offering to the medical profession a review of the important articles which have appeared in the literature during the past year. As would be expected because of the war, there has been a relative scarcity of foreign material. Approximately 28 per cent of the articles reviewed in this volume come from outside of the United States. As one scans through the pages of this volume he is impressed by the immense amount of work which is required to assemble the material. As in previous years the authors present the material in a concise but easily readable manner. Merely paging through the book will review one's reading for the past year and will no doubt reveal a number of articles which have escaped attention, making the book invaluable for reference work.

In the field of radiological diagnosis the authors have been reluctant to choose any particular work as outstanding but mention a number of interesting and refreshing subjects. Articles of interest on the osseous system include changes in the epiphyses found in observing hyperthyroid children, "pseudo-fractures" as related to faulty nutrition and military service, injuries following metrazol therapy, solitary eosinophilic granuloma, and porotic conditions. The use of organic salts of iodine in bronchography, the results of mass surveys for tuberculosis and "virus" or "type X" pneumonia, are important contributions. In the field of gastroenterology considerable attention is being given to the small bowel. The use of the Miller-Abbott tube in intestinal obstruction, and a new dye, phenyl propionate acid, for the study of the gall bladder, are subjects of more than ordinary interest.

In the introduction to the section on radiotherapeutics, Dr. Kaplan has given a very excellent, concise, and interesting review of the progress in this field during the past year. Because of the war there has been a transition from old to new world dominance in the field of medical radiology. In some countries research centers have been entirely destroyed, while in others the chief emphasis has been placed on scientific achievements associated with military needs. Because of the destruction of hospitals and medical centers in England it has been necessary to rely more and more upon radium, particularly radon, rather than x-ray therapy. There has been continued interest in the treatment of nonmalignant lesions. A number of articles have appeared on the use of supervoltage therapy as compared to the conventional 200 kilovolt type. The question of whether tuberculosis can be treated by x-ray again is receiving some attention but the answers have been either cursory or negative. The question of preoperative x-ray therapy for carcinoma of the breast is still unsettled, possibly because of the great variations in methods and technique. The value of ovarian irradiation, in breast carcinoma and metastases, has received considerable attention during the past year. Paging through this section one is impressed by the great amount of work which is being carried out, particularly in the United States.

It is hoped that in spite of the interruption of the work in foreign medical centers and the currently disordered world, it will be possible for the authors and publishers to see their way clear to continue the publication of this excellent yearly review of international literature. As the reviewer has stated in previous years, he finds this volume indispensable in his work and ventures to say that this is the feeling of the great majority of radiologists throughout the country. EARL E. BARTH.

[1] THE 1941 YEAR BOOK OF RADIOLOGY. DIAGNOSIS edited by Charles A. Waters, M.D., and Whitmer B. Firor, M.D. THERAPEUTICS edited by Ira I. Kaplan, B.Sc., M.D. Chicago: The Year Book Publishers, Inc., 1941.

THE general scope and plan of the second edition of Kracke's *Hematology*[1] is similar to the first edition. (Reviewed in this Journal in the May, 1938, issue on page 944.) The material is grouped in eight sections as follows: (1) hematologic terminology, (2) the development and morphology of blood cells, (3) leucocytosis and leucopenia, (4) the anemias, (5) the leucemias, (6) hemorrhagic diseases, (7) miscellaneous, and (8) hematologic technique. The volume has been enlarged by 160 pages in order to include many of the advances in hematology during the last four years. There are new chapters on hemoglobin and its derivatives and the porphyrin compounds, the hemolytic anemias and hemoglobinuria. The table of the more common injectable liver extracts with their potency and cost will be helpful in choosing therapy for the patient with pernicious anemia. Dr. Lloyd Craver has contributed an excellent chapter on the treatment of leucemia in which is included the use of radioactive isotopes. Other new chapters are those on vitamin K and Hodgkin's disease. Subjects of current interest also added are the operation of a blood bank, plasma transfusion, and the effect of the sulfonamides on the blood picture.

Drawings of leucocytes in several new colored plates show much greater detail and are more realistic than in the older plates.

It is felt that the section on the anemias would be improved by closer adherence to an etiological classification. In the description of the anemias, very little reference is made to cell measurements such as corpuscular volume, corpuscular hemoglobin, and hemoglobin concentration.

The complete bibliography at the end of each chapter is a very useful feature. This unique volume should continue to be a valuable reference book to physicians confronted with hematologic problems.

HOWARD L. ALT.

[1] DISEASES OF THE BLOOD AND ATLAS OF HEMATOLOGY. By Roy R. Kracke, M.D. 2d ed. Philadelphia, London, Montreal: J. B. Lippincott Co., 1941.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

AIDS TO ANAESTHESIA. By Major Victor Goldman, L.R.C.P., M.R.C.S., D.A., R.A.M.C. London: Baillière, Tindall and Cox, 1941.

SURGERY OF THE AMBULATORY PATIENT. By L. Kraeer Ferguson, A.B., M.D., F.A.C.S. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1942.

THE PRINCIPLES OF NEUROLOGICAL SURGERY. By Loyal Davis, M.S., M.D., Ph.D., D.Sc., (Hon.). 2d ed. Philadelphia: Lea & Febiger, 1942.

ANAESTHETICS AFLOAT. By Surgeon Lieutenant Commander Ronald Woolmer, R.N.V.R., B.A., B.M., B.Ch. (Oxon.), D.A. London: H. K. Lewis & Co. Ltd., 1942.

PEDIATRIC GYNECOLOGY. By Goodrich C. Schauffler, A.B., M.D. Chicago: The Year Book Publishers, Inc., 1942.

A TEXTBOOK OF SURGERY BY AMERICAN AUTHORS. Edited by Frederick Christopher, B.S., M.D., F.A.C.S. 3d ed. Philadelphia and London: W. B. Saunders Co., 1942.

NEURO-ANATOMY. By Walter R. Spofford, B.S., Ph.D. Oxford Medical Outline Series. London, New York, Toronto: Oxford University Press, 1942.

MINOR SURGERY. By Charles M. Oman, M.D., F.A.C.S. Oxford Medical Outline Series. London, New York, Toronto: Oxford University Press, 1942.

A TEXTBOOK OF THE PRACTICE OF MEDICINE. Edited by Frederick W. Price, M.D., C.M., F.R.C.P., F.R.S (Edin.). 6th ed. London: Humphrey Milford (Oxford University Press), 1941.

LANE MEDICAL LECTURES: THE LYMPHATIC SYSTEM; ITS PART IN REGULATING COMPOSITION AND VOLUME OF TISSUE FLUID. By Cecil K. Drinker. Stanford University Publications, University Series. Medical Sciences, Vol. 4, No. 2. Stanford University, Calif.: Stanford University Press, and London: Humphrey Milford (Oxford University Press), 1942.

MÉTODOS MODERNOS DE AMPUTAÇÃO. By Edmundo Vasconcelos. São Paulo: Companhia Editora Nacional, 1942.

VAGINAL HYSTERECTOMY. By James William Kennedy, M.D., F.A.C.S., and Archibald Donald Campbell, M.D.C.M., F.R.C.S., (C), F.R.C.O.G., F.A.C.S. Philadelphia: F. A. Davis Co., 1942.